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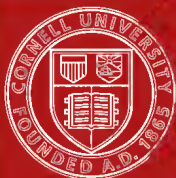
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A LABORATORY MANUAL
OF
ORGANIC CHEMISTRY



A LABORATORY MANUAL
OF
ORGANIC CHEMISTRY

A COMPENDIUM OF LABORATORY METHODS
FOR THE
USE OF CHEMISTS, PHYSICIANS,
AND PHARMACISTS

BY
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TRANSLATED, WITH THE AUTHOR'S SANCTION, FROM THE
SECOND GERMAN EDITION BY

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London
MACMILLAN AND CO.
AND NEW YORK

1895

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TRANSLATOR'S PREFACE

THE book which is herewith presented in English translation has met with such success in the original language that a second edition was called for in less than three years from the date of its first publication. It covers a field not previously occupied, and the fact that the first edition has appeared in a French dress leads to the hope that a welcome may likewise be extended to an English version. The translation has been made from the second edition (1893).

The work does not take the place of any of the text-books of organic chemistry, but bears towards them the relation of an almost indispensable complement. Most text-books deal mainly with the description of substances and of chemical reactions. The present volume is a compendium of the methods actually used in the laboratory in the prosecution of organic work.

To render the book more easily available for rapid reference, a few modifications have been introduced by the translator with the approval of the author. The classification according to subject of the contents of each chapter, and the division into numbered sections with conspicuous headings, have involved no alterations beyond occasional slight rearrangements

in the order of the paragraphs and should greatly facilitate the finding of any particular method. In connection with this, a detailed table of contents has been supplied in place of a bare list of the titles of the chapters. This seemed an especially desirable change inasmuch as the index, although it has been made as complete as possible, could not, in the very nature of the case, enable the reader to make the fullest use of the book. He would be more likely to take up the volume in order to get suggestions along a certain line, than information on a specific point.

A number of matters of subordinate interest, and methods differing but slightly from others previously described, have been printed in smaller type in order to relieve the main text of details which might otherwise overcrowd and confuse it.

Beyond these, very few changes from the original have been made, and since they have all been carried out in consultation with the author, and sometimes at his suggestion, it has not been thought necessary to designate them particularly in the text. With the exception of some half dozen, they have been insignificant.

In a few places, references to papers published within the last two years have been added. New reactions and new substances are discovered in large numbers every year, but new methods of work are devised in much less rapid succession, so that a book of the nature of the present is less in danger of becoming out of date than an ordinary text-book. More extensive changes, with the view of correcting this tendency of most chemical works, were therefore unnecessary.

The references to the original literature are a valuable feature of the book. These have all been verified, as far as the sources were accessible, and a number of errors have been corrected. While it can hardly be hoped that perfection has

been attained, every care has been taken in securing substantial accuracy in this particular.

To render easier the use of the abstracts published in the *Berichte der deutschen chemischen Gesellschaft* or the *Journal of the Chemical Society* by those who have not access to other journals, a concise table, showing the year of publication of each volume of the periodicals mentioned, has been inserted as an appendix. The paper will usually be found in the volume of abstracts for the year of its publication, or at all events in that for the following year.

In conclusion the translator desires to extend his sincerest thanks to Mr. J. B. Garner for his kind and valuable assistance in revising the proof sheets, and to several friends to whom he owes useful suggestions.

THE TRANSLATOR.

UNIVERSITY OF CHICAGO,
April, 1895.

AUTHOR'S PREFACE TO THE FIRST GERMAN EDITION

IN consequence of the comparative ease with which the operations of inorganic chemistry can be carried out, we commonly find all the necessary general instructions, as well as the details of particular operations, given with sufficient fulness even in the smaller books on the subject. The textbooks on organic chemistry, however, usually treat the practical side of the science in a very perfunctory manner. The reader may even get the impression that there are no difficulties in the way of realising the actions expressed in the most complicated equations, and that the yields calculable from the equations will invariably be attained in practice.

Theoretically nothing can be simpler than the preparation of an ester. It is formed from an acid and an alcohol, and water is eliminated in the process. But the student soon finds that the largest attainable yield of ester can only be reached in the laboratory when certain definite conditions are rigidly observed.

It is conceded that the discovery of methods which will give quantitative yields is as much expected of the worker in organic

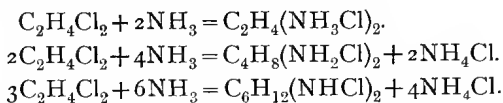
as in inorganic chemistry. Indeed the very satisfactory processes used in the technical preparation of organic bodies show that this ideal can frequently be reached. It is true also that in many interactions several chemical changes take place simultaneously, and here we may take the sum total of the products as representing the yield. This will be the case, for example, where, in dealing with substances having a constitution represented by atoms or groups of atoms arranged in a closed chain, a number of isomeric derivatives may be produced by the action of one reagent. But how often it happens that only two or three per cent. of the material used is transformed into what we regard as the chief product, and we remain entirely in ignorance of the fate of the bulk of the interacting substances.

The fundamental rule of submitting various substances to chemical change in molecular proportions by weight, in order to limit the opportunities for subsidiary actions, is not always adhered to in practice. Indeed there must be exceptions to this, as to every rule, particularly if the expression is restricted to cases in which one molecular proportion of a body is brought in contact with not more than four such proportions of another. The difference which a wider interpretation of the rule may make in the ultimate yield is strikingly illustrated by the following example.

It had been shown by Hofmann (*Ber.* **4**, 667) that by the action of excess of alcoholic ammonia on ethylene chloride at 100–120°, only about 5 per cent. of ethylene diamine hydrochloride was formed. The product contained large amounts of bases of more complicated constitution.

Kraut (*Ann.* **212**, 251) re-examined the matter and found that, in accordance with Hofmann's results, 2.5–3 molecular proportions of ammonia to one of ethylene chloride gave a small quantity of the ethylene diamine salt and nearly 73 per

cent. of ammonium chloride. He offered the following equations in explanation of the action :



The formation of the product sought involved the production of no ammonium chloride, while that of the hydrochlorides of diethylene diamine and triethylene diamine led to the formation of 54.04 and 72.05 per cent. respectively of this by-product. It was evident therefore that the ethylene diamine first produced had been for the most part altered by further chemical changes.

In addition to this, Kraut observed that the product of the action of ethylene chloride on three molecular proportions of alcoholic ammonia, after it had cooled, contained free ethylene bases whose formation was accounted for by the equation :



The ammonium chloride survived the action only in virtue of the fact that it crystallised out of the alcoholic solution. In the absence of alcohol, water being used in its stead, when the liquid was evaporated the hydrochloric acid united with the less volatile ethylene bases and the ammonia was driven off. In the first stages of the interaction, therefore, free ammonia and free ethylene diamine were both present. The action of fresh ethylene chloride on these produced ethylene diamine and diethylene diamine, and the greater the amount of ammonia present, the greater would be the extent to which the former would be produced in proportion to the latter.

Kraut therefore heated ethylene chloride (1 mol.) and 33 per cent. aqueous ammonia (18 mol.) in a sealed tube for five

hours at $115-120^{\circ}$, and obtained 95 per cent. of the theoretically possible yield of ethylene diamine.

Of recent years several works have appeared in which all the methods for the preparation of certain classes of bodies are collected. But even these confine themselves almost entirely to the statement of the equations representing the chemical actions. By using the numerous references to the literature which they contain, it is easy for the reader who has access to an adequate library to ascertain the exact course which was followed in any particular case. In the present volume, on the other hand, an effort has been made to bring together the methods which may be employed for carrying out all the common operations, such as sublimation, reduction, and the preparation of nitro-bodies and of sulphonic acids, without reference to the particular substances employed. Care has been taken also to show by means of examples how various investigators have overcome the difficulties of any particular case. It was not possible of course to give all the methods that have ever been used. The attempt has been made, however, to give a sufficient selection, and the material has been drawn from all accessible foreign, as well as German, sources.

The possible variations in methods of work are as inexhaustible as the science of chemistry itself. Every day brings its novelty and an exhaustive treatment of such a subject is impossible. But those who have not had, or do not have, time to read extensively in chemical literature will find here collected all that is essential in the large volume of experience in the practice of organic chemistry which is scattered and hidden in the great stores of published matter. Thus one who, for example, attempts all reductions by means of tin and hydrochloric acid and similar agents may find in the following pages methods which will suit his purpose

better; or be led to their discovery by the study of cases similar to that with which he is dealing, which may be cited in the text. Its object will have been attained if the book encourages work in the field of organic chemistry and lightens the labour of the workers.

THE AUTHOR.

KÖNIGSBERG,
May, 1890.

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ABBREVIATIONS

- A. Path. Pharm. = Archiv für experimentelle Pathologie und Pharmakologie.
Am. Ch. J. = American Chemical Journal.
Ann. = Liebig's Annalen der Chemie und Pharmacie
Ann. Ch. Ph. = Annales de Chimie et de Physique.
Ar. Pharm. = Archiv der Pharmacie.
Ber. = Berichte der deutschen chemischen gesellschaft.
Bull. Ch. = Bulletin de la Société Chimique de Paris.
C. R. = Comptes rendus de l'Académie des Sciences (Paris).
Centralblatt = Chemisches Centralblatt.
Ch. N. = Chemical News.
Ch. Z. = Chemiker-Zeitung.
D. P. J. = Dingler's Polytechnisches Journal.
Ger. Pat. = German Patent.
Jahresb. = Jahresbericht über die Fortschritte der Chemie.
J. Ch. Soc. = Journal of the Chemical Society (London).
J. pr. Ch. = Journal für praktische Chemie.
M. f. Ch. = Monatshefte für Chemie.
P. Ar. = Pflüger's Archiv für die ges. Physiologie.
Z. analyt. Ch. = Zeitschrift für analytische Chemie.
Z. angew. Ch. = Zeitschrift für angewandte Chemie.
Z. Bio. = Zeitschrift für Biologie.
Z. Ch. = Zeitschrift für Chemie.
Z. physik. Ch. = Zeitschrift für physikalische Chemie.
Z. physiolog. Ch. = Zeitschrift für physiologische Chemie.

PART I

GENERAL METHODS

CHAPTER I

BATHS

1. General Remarks.—Baths are used in order to heat vessels more uniformly than is possible with the naked flame. Among the kinds employed are water, salt, saltpetre, and chloride of calcium baths. The last named substance attacks copper very vigourously on prolonged exposure to the boiling solution of the salt. A saturated solution of common salt boils at 180° (Gerlach, *Z. analyt. Ch.* **26**, 427), a saturated sodium nitrate solution at 120° , and a saturated chloride of calcium solution at 180° (Legrand, *Ann.* **17**, 34).

2. High Temperatures.—By the use of oil, paraffin, or sulphuric acid high temperatures may be attained. Metal baths are however preferable to any of these, as the disagreeable odours of the two first and the pungent odour of the last substance are entirely avoided, and the use of a hood is rendered unnecessary. These baths are made of easily melted alloys. For high temperatures lead contained in a cast-iron vessel may be employed. Smith and Davies (*J. Ch. Soc.* **37**, 416) recommend that, in using such a bath, the part of the flask which dips into the lead should be covered with lampblack, from a smoky flame, as this prevents the lead adhering to the glass and makes the vessel less liable to crack.

3. Dry Baths and Air Baths.—Dry baths are shallow iron basins containing a little sand ; the quantity of the latter should be small on account of its low conductivity for heat. Sometimes graphite and iron filings are used in place of sand. Such baths are applicable where materials are to be boiled for days in connection with a reflux condenser. Even where the liquid is alcohol or ether, their use is advisable, since all attention to keeping a constant level, as in a water bath, is avoided.

Air baths are extremely useful for all purposes, especially in the form which Lothar Meyer (Ber. **22**, 879) has recently given to them. It is unnecessary to describe them, as they cannot be constructed in the laboratory, and should be bought ready made.

Where it is necessary to evaporate ether and other easily inflammable substances, the tripod stand should be surrounded with fine-meshed wire gauze. This application of the Davy safety lamp effectually prevents ignition of the vapour.

CHAPTER II

CRYSTALLISATION

1. Solvents.—The crystallisation of organic substances is effected by dissolving them in suitable solvents. A hot saturated solution of the substance is prepared, which, on cooling, deposits the dissolved material in crystalline form. Immersion in a freezing mixture, such as equal parts of snow and salt, producing a temperature of -17° C., or of snow and chloride of calcium, producing -48° C., is sometimes necessary. Many solvents remain perfectly liquid at these temperatures. Carbon disulphide, for example, freezes at -116° C., 95 per cent. alcohol at -130° C., and pure ether probably demands a still lower temperature (Ber. **10**, 831). Crystallisation may likewise be brought about by permitting the solvent to evaporate. With the exception of sublimation, other methods of obtaining crystals are seldom used in organic chemistry.

The following substances, or suitable mixtures of two or more of them, are used as solvents; but their application in any particular case is regulated by the requirement that they must have no chemical action on the substance to be dissolved:—

Acetic acid.

Acetic ether.

Acetone.

Alcohol and its homologues.

Ammonia water.

Benzene and its homologues,

Toluene, Xylene,¹ and

Cumene.²

Carbon disulphide.

Chloroform.

Ether.

Hydrochloric acid.

Naphthalene.

Nitric acid.

Nitrobenzene.

Petroleum ether.

Phenol.

Pyridine.

Sulphuric acid.

Water.

Ber. **25**, 185c.

² Ber. **17**, 2,812.

The following are occasionally employed: Aniline (for indigo and naphthylamine, Ber. **3**, 289); Azobenzene (Ber. **23**, 184); Canada balsam, or rosin, for the study of crystallisation under the microscope (Ber. **23**, 1,747); Kerosene (Ber. **24**, R. 652); Cresol; Dimethylamine (Ber. **25**, 2,008); Glycerol (Ger. Pat. 46,252); Hydrofluoric acid (Ber. **12**, 581); Isobutyl alcohol (Ber. **20**, 3,275); Olive oil (much used as a harmless solvent for substances to be given to animals by subcutaneous injection); Paraffin (Ber. **25**, R. 488); Petroleum (Ber. **24**, 2,597); Phosphorus oxychloride (Ber. **18**, R. 22); Sodium hydroxide solution (Ber. **24**, 2,714); Spermaceti (Ber. **4**, 334); Turpentine.

In reference to the various solvents a few remarks may be made.

When glacial or common *Acetic acid* has been used for recrystallisation, it is advisable, if possible, to free the substance from traces of the solvent by passing a stream of air over it in a Liebig's drying tube at 100°, or to let it stand in vacuo over soda-lime (Ann. **228**, 303). It is usually sufficient, however, to let the acetic acid evaporate in an ordinary desiccator charged with potassium hydroxide (Ber. **14**, 1,867). Acetic acid of crystallisation was found by Latschinoff (Ber. **20**, 1,046) in the case of choleinic acid, $C_{25}H_{42}O_4 + C_2H_4O_2$. Crystals of haemin are likewise said to retain some acetic acid (A. Path. Pharm. **20**, 328).

Acetone is being found more and more useful as a solvent every day. Cholic acid crystallises from it with one molecule of acetone of crystallisation.

That *Alcohol* can enter into combination as alcohol of crystallisation was first noticed by Graham, and, although the observation attracted not only notice but contradiction, it has since been confirmed (Ann. **65**, 120). Hesse seems to have found in conchairamine (Ann. **225**, 247), $C_{22}H_{20}N_2O_4 + H_2O + C_2H_6O$, an alkaloid occurring with quinine, the only example of a substance crystallising with both water and alcohol. In the barium salt of choleinic acid, Mylius (Ber. **20**, 1,970) met with the unusual case of a substance which will not dissolve either in water or absolute alcohol, but is easily soluble in dilute alcohol.

A partial transformation of organic acids into esters is sometimes effected by mere boiling with alcohol. This action cannot be considered as a method of preparing esters, but it is occasionally encountered in recrystallising acids from alcohol. In the case of cholic acid, for example, a very large proportion seems to disappear in the alcoholic mother-liquors, considerable quantities of which

result from the crystallisation. The author (Ber. **25**, 807, and Z. physiolog. Ch. **16**, 497) has shown that it is converted into the more soluble ethyl ester. Where acids with such properties are met, acetone, benzene, etc., are used in order to avoid the difficulty.

Certain substances are equally soluble in hot and cold, or even cold dilute alcohol, although insoluble in water. They can often be obtained in a crystalline form by evaporating the alcoholic solution, after the addition of much water, on the water bath until a slight turbidity appears. The crystals separate on cooling. Frequently the alcohol must be of a definite strength. Kiliani (Ber. **24**, 339) found, for example, that digitonin crystallised perfectly from 85 per cent. alcohol, while the yield from stronger spirit was amorphous, and from weaker spirit was smaller in quantity and mostly amorphous.

According to Herzfeld (Ber. **12**, 2,120), it seems to be necessary to exercise special care in the case of maltose. The crystallisation is best carried out by dissolving it in hot 80 or 85 per cent. alcohol, letting the solution stand for some time in the cold in a closed vessel, and then allowing the alcohol to evaporate. This process may be explained by supposing that maltose turns into a deliquescent hydrate on heating, and only returns to the state of anhydride on long standing.

The acid sodium salts of many organic acids can only be crystallised by dissolving them in absolute alcohol and adding ether, the precipitate produced becoming crystalline in the course of a few days. It is in this way, for example, that, as Plattner first showed, the so-called crystallised bile can be obtained. It is a mixture of sodium taurocholate and glycocholate.

It occasionally happens that acidified is preferable to neutral alcohol. A few drops of acetic or some other acid are used. Caffein sulphate was held to be a very difficult substance to prepare until Biedermann (Ar. Pharm. **1883**, 181) found that this salt could be obtained in crystals with extraordinary ease by dissolving the alkaloid in about ten times its weight of hot alcohol, which had been strongly acidified with sulphuric acid, and allowing the solution to stand for some time in a cool place.

Many substances which tend to separate out in amorphous form may be obtained in a crystalline condition by the use of a mixture of water, alcohol, and ether, a method which is less used than it deserves. Parthiel (Ber. **24**, 636) prepared cystine hydrobromide from the concentrated aqueous solution of the base by neutralising

with 25 per cent. hydrobromic acid, and obtained it from the solution by adding absolute alcohol and covering with a layer of ether. According to Bayer (Z. physiolog. Ch. **3**, 303), if water is added to an alcoholic solution of cholic acid till it is permanently turbid, and ether is then poured on the surface, the acid comes out in clumps of crystals.

Amyl alcohol (cf. Chap. VI., § 2) is an excellent solvent for substances which can hardly otherwise be obtained in crystalline form. For example, Niementowsky (J. pr. Ch. **148**, 22) used it to dissolve *m*-methyl-*o*-uramidobenzoyl, which is difficultly soluble in all solvents, and needles came out on cooling the solution.

Haemine hydrochloride, made from red blood-corpuscles, crystallises, according to Nencki (A. Path. Pharm. **20**, 328), with one molecule of alcohol of crystallisation, $C_{32}H_{31}ClN_4FeO + C_5H_{12}O$.

Benzene can enter into combination as benzene of crystallisation and may be held very tenaciously. Thrular (Ber. **20**, 669) found that thio-*p*-tolylurea did not completely lose its three molecules of benzene even after heating for four hours at 100–110°. Liebermann and Limpach (Ber. **25**, 325) recrystallised tropine from benzene, and endeavoured, by heating to 70°, to determine the amount of the latter present in the crystals. As, however, the weight refused to become constant, owing to volatilisation of the tropine itself, they convinced themselves of the absence of benzene of crystallisation by determining the nitrogen in a freshly prepared specimen. Kishner (Ber. **24**, R. 559) states that triphenylbenzene unites with benzene in such a way that if it is warmed with a solution containing the latter, and allowed to crystallise, it takes the benzene down with it. He uses this as a method for separating benzene from other substances.

As Liebermann and Seyewitz (Ber. **24**, 788) have shown, commercial benzene (boiling point 80–82°) contains from 0·2 to 0·3 per cent. of carbon disulphide, which in certain cases leads to undesirable secondary reactions. It is best removed by shaking with concentrated alcoholic potassium hydroxide, which converts the impurity into potassium xanthate, and redistilling.

Chloroform is found combined in crystals. The triazine of benzene (Ber. **20**, 325), $C_{27}H_{18}N_6$, crystallises with one molecule of chloroform, colchicine (M. f. Ch. **7**, 571) with two, leukon-ditoluylene-chinoxalin (Ber. **19**, 776) with one, which is completely expelled only at 140°, and Schmidt found it so firmly held in berberine-chloroform, $C_{20}H_{17}NO_4CHCl_3$ (Ar. Pharm. **1887**, 147),

that he doubts the presence of a mere addition product containing the components unchanged.

Chloroform usually contains a little alcohol, and may be freed from it by washing with water. Contrary to ordinary experience, Oudemans (Ann. **166**, 74) found that cinchonine was more soluble in a mixture of alcohol and chloroform than in either of the constituents.

Ether appears in exceptional cases as ether of crystallisation. Fischer and Zeigler (Ber. **13**, 673), for example, obtained crystals of pseudo-leukaniline containing ether. It is advisable to dry ethereal solutions with chloride of calcium before setting them aside to crystallise, as otherwise the crystals will be damp from the water left by the moist ether on evaporation.

Commercial ether has usually an acid reaction (Ber. **24**, 1,491). It may be purified by shaking with sodium hydroxide and subsequently with water. If it is tested after standing for a long time, it will be found to contain traces of acid once more.

Many substances do not crystallise out of water unless their solution is covered with a layer of ether. In order to obtain crystalline glycocholic acid from ox-gall—the gall of oxen from the neighbourhood of Tübingen is used, as that from other districts contains too little—the gall is placed in a narrow cylinder, covered with ether, and 1 cc. of concentrated hydrochloric acid is added for each 20 cc. of ether. The crystals appear after the whole has stood for several days.

Warm *hydrochloric acid* is often very useful, as many resinous matters are insoluble in it. For instance, in recrystallising crude para-nitrophenol from it the resin remains undissolved, and the same is true of meta-bromonitrophenol (Ber. **25**, 552).

Nitrobenzene was used by Gabriel (Ber. **19**, 837) for recrystallising nitroacetylene-diphthalide, which comes out of it in thick needles. Gräbe and Philips (Ber. **24**, 2,298) used nitrobenzene, or a mixture with acetic acid, for recrystallising some of the series of dyes which are obtained by successive additions of hydroxyl groups to alizarin when it is heated with sulphuric acid (see Chap. XVIII. "Oxidation").

Naphthalene was used by Witt for recrystallising naphthazine, as it cannot otherwise be obtained in crystals. It was dissolved in the boiling hydrocarbon, and the solid cake was afterwards extracted with hot alcohol until only the azine in crystalline form remained. It is stated in a patent-

specification (Ger. Pat. 59,190) that nitro-alizarin blue, which is difficultly soluble in ordinary solvents, may be recrystallised from naphthalene.

For *Petroleum ether* it is best to use the fraction of the commercial product which distils over between 60° and 70° on the water bath (Ber. **23**, 142). Wislicenus (Ann. **272**, 19) names the part which comes over, after repeated rectification, between 33° and 39° petroleum-pentane, and the part between 60° and 69° petroleum-hexane.

Nötling and Schwarz (Ber. **24**, 1,606) dissolved crude triquinylmethane in the smallest possible quantity of benzene, and added petroleum ether, of boiling point under 100° , to the solution. They used petroleum ether which had been purified by treatment with sulphuric acid and distillation because the commercial product gave nothing but tar. As soon as the precipitate produced by the ether was no longer resinous they filtered, and, after adding a little more of the ether, allowed the solution to crystallise over paraffin and sulphuric acid.

Phenol, which is an excellent solvent although it has been too little used for purposes of crystallisation, was employed by Witt (Ber. **19**, 2,791) in the following way in order to obtain crystalline eurhodol, a substance which is left untouched by all known solvents. He dissolved the hydrochloride of the base in phenol, and, after cooling to 100° , added boiling alcohol with which a little aniline had been mixed. The aniline neutralised the hydrochloric acid and eurhodol began to separate out in needles.

The phenol which remains adhering to the crystals may be removed by washing with alcohol. It is met with also as phenol of crystallisation, as for instance with urea (Ar. Pharm. **1886**, 625) and cholic acid (Ber. **20**, 3,278).

Pyridine seems to be a specially useful solvent for the recrystallisation of substances of the class of chlorinated benzidine and tolidine derivatives, which are scarcely soluble in other solvents (Böttinger, Dissert. Jena, 1891).

Concentrated *sulphuric acid* may be used where all other solvents fail. Baeyer obtained bichloro-hydurilic acid in crystalline form with its help by dissolving the substance in the concentrated sulphuric acid and adding water cautiously. Many sulpho-acids, like Lönies' γ -sulphoisophthalic acid (Ber. **13**, 704), which come out of water in the form of resin, are easily recrystallised from dilute sulphuric acid.

Where *water* is used for the recrystallisation of substances on which the oxygen of the air may act, as for example amines which are coloured by its action, some hydrogen sulphide or sulphurous acid may be added.

Water of crystallisation is found in the most various proportions. For example, some carbohydrates contain one sixth of a molecule, phenyldihydro- β -naphthotriazin (Ber. **24**, 1,003), two thirds of a molecule, and so forth. Such water is sometimes held with extraordinary tenacity; in the case of the barium salt of an acridone sulphonc acid the one and a half molecules can be driven off only at 220° (Ber. **25**, 1,981).

The case of citric acid is very extraordinary in this respect (Ber. **25**, 1,159). According to Witter, if its solution is evaporated till the temperature reaches 130° , the acid crystallises out on cooling free from water, and the product may be recrystallised from cold water without change. If however a crystal of ordinary citric acid, containing water of crystallisation, be inserted into the solution, crystals containing water come out. This unusual property is not destroyed by conversion into the lead salt, as is shown by the properties of the acid when it is once more set free.

In connection with the foregoing it may be worth mentioning that a cold saturated solution of *borax* is sometimes useful as a solvent, especially for colouring matters which are insoluble in water. For example, after the tannin has been extracted from sandalwood by means of water, a solution of borax extracts the santalin, and the latter may then be precipitated from solution with sulphuric acid. Investigations in this direction are due to Palm (Z. analyt. Ch. **22**, 324).

2. Filtration and Precipitation.—In *filtering hot saturated solutions* a hot water funnel must be used, as otherwise crystals are apt to form and stop up the funnel. If the quantity of the solution is small the funnel can be warmed directly in a flame before the filter-paper is placed in it. Where suitable filter-paper is used, this is almost always sufficient to prevent crystallisation either in the stem of the funnel or in the funnel itself.

It is not always best to wait for the complete cooling of the crystallising solution. Crystallised veratrine can be obtained easily and in good yield, according to Schmidt and Bosetti (Ar. Pharm. **1883**, 84), only by dissolving the commercial alkaloid, after it has been purified with ether, in a large beaker in absolute alcohol, heating to $60-70^{\circ}$, and adding water

till permanent turbidity appears. This is cleared up with a little more alcohol and the whole allowed to evaporate at 60–70°. The veratrine crystallises out plentifully in a nearly pure condition. The moment the solution begins to become turbid by the separation of the resinous modification, the liquid is poured off the crystals. The operation may be repeated several times with the liquid, and a total of about 33 per cent. of the base obtained pure.

Precipitation by the addition of a salt to water solutions is a method frequently applied. It is used with solutions of both solids and liquids, and its action depends on the fact that the addition of the salt produces a liquid in which the substance can no longer remain dissolved. Common salt, Glauber's salt, and potassium carbonate are thus used. For example, the addition of potash to water containing alcohol causes the latter to separate out in a layer on the surface.

Separations which are of great importance in the chemistry of albuminous substances may also be carried out in this way. Ammonium sulphate is used for separating albumens from peptones (albumen derivatives which have been altered by digestion and are no longer coagulated by boiling water). The former are insoluble in solutions containing ammonium sulphate, and so are precipitated by the addition of a solution of that salt (Z. Bio. **22**, 423). Such separations play a decisive part in this department of chemistry, and many regard them as quantitative, although no one has yet obtained unassailable proof that they are so (see below). On the other hand the method is naturally admirable where the substance can only be obtained pure with great difficulty in any other way, and subsequent recrystallisation proves that this has given a pure product. Baeyer (Ber. **12**, 1,317), for example, dissolved amido-indigo in dilute hydrochloric acid, neutralised with soda and reprecipitated with sodium acetate. In a similar manner he purified ethyl amido-phthalate (Ber. **10**, 1,079).

Precipitation from alcoholic solutions by means of water has already been referred to. It is frequently found that a substance which is very soluble in alcohol and not soluble in water, can be induced to crystallise by adding water to the alcoholic solution till a faint turbidity appears. The method is however much more frequently applied to ethereal solutions, in which case, as many bodies are insoluble in petroleum ether while soluble in ether, the former is added till slight turbidity is noticed. Phenol solutions may be similarly diluted with alcohol (Ber. **27**, 2,403).

Crystals are freed from the mother-liquor by washing. Where a large quantity of material is to be treated, it is put into a funnel and

a water pump is used. If the liquid is strongly alkaline or strongly acid it is preferable to use a glass bead, with or without paper, instead of a platinum cone.

If there are very few crystals, and especially if the accompanying liquid is thick, they are spread on unglazed porcelain to dry. Bisque plates, which are damaged and useless for making china, are very suitable. In their absence any kind of tile which will absorb the mother-liquor may be used. The crystals may also be pressed between filter-paper, although the results are less satisfactory in this case. If the mother-liquor is of value it may be recovered from the porcelain or paper by extraction.

3. Recrystallisation.—*To obtain chemically pure substances* is the object of recrystallisation. If this is not accomplished the first time, the operation is repeated till the material is pure, and all the impurities are collected in the mother-liquors. The assumption is that mixtures of crystals may be separated by their different solubilities in different media; that, in fact, with a suitable amount of the solvent more of the one substance than of the other will remain in the mother-liquor. As a matter of fact, substances which cannot be separated by fractional crystallisation have been found almost exclusively among thiophene derivatives. Cohn (Z. **17**, 306) has lately made the interesting observation that if molecular quantities of *p*-nitrobenzoic acid and *p*-acetylamidobenzoic acid are dissolved in hot water, they crystallise out together on cooling and cannot be separated again by crystallisation alone. Mixed crystals in the ordinary sense are frequently mentioned in chemical literature. Herrmann (B. **19**, 2,235) found, for example, that succino-succinic ether and quinone dihydro-carboxylic ether, although the former is asymmetric and the latter rhombic, formed mixed crystals.

Inoculation (Z. physiolog. Ch. **10**, 151), with a crystal from another lot of the same substance, is a frequent means of causing oils to crystallise, but this is not always available. Städel has found however that a crystal of the same substance is not always absolutely necessary; that a fragment of a substance of similar constitution is sometimes effective in starting crystallisation. Thus he took *m*-kresol, which is said not to solidify at -80° , and rendered it crystalline by adding a minute crystal of phenol. Ott (B. **24**, 2,603) states that the dibromide of propylidene-acetic acid refuses to crystallise, but may be induced to do so by infecting it with a crystal of the dibromide of ethylidene-propionic acid.

Fractional recrystallisation is the name given to the operation when it has to be repeated frequently and guided in a particular direction so as to lead to a chemically pure product. An example will best illustrate how, *mutatis mutandis*, one should proceed in such a case.

Schwalb (Ann. **235**, 110) saponified bees-wax with sodium hydroxide and extracted the dry soap with petroleum ether. The non-acid products of the saponification were submitted to fractional crystallisation in such a way that the higher-melting fractions were always recrystallised from fresh petroleum, while for the lower-melting part the mother-liquor of the next higher-melting fraction was used. In this manner the low-melting substance accumulated in the mother-liquors, while high-melting material appeared in first quantities of crystals. This systematic method was pursued until the melting point of the crystals no longer differed appreciably from that of the substance obtained by the evaporation of their mother-liquor. As soon as this point was reached this portion of crystals was set aside for further treatment, and the recrystallisation of the still impure middle fractions was continued. In this way three principal portions were obtained, and these were then separately submitted to the same process. Besides many other products, a substance which on analysis seemed to be a hydrocarbon was obtained. But before the melting points of the crystals and the deposit from the mother-liquor agreed, it was necessary to recrystallise this product alone thirteen times more.

The only way by which Zinoffsky (Dissert. Dorpat, 1885) was able to determine that oxyhaemoglobin from horse's blood, purified by recrystallisation, was really a pure substance, was by ascertaining that the percentages of iron in the crystals and in the residue from evaporation of the mother-liquor were identical.

It is hardly possible to obtain the oxyhaemoglobin from the blood of some animals in a pure condition. To this class belongs that of swine Höffner (Z. physiolog. Ch. **7**, 67) made the extraordinary discovery that if defibrinated blood from this species was treated with one third of its volume of a 1 per cent. alcoholic solution of quinoline and then placed in a freezing mixture, it changed in a few days into a mass of red crystals. Otto has followed up this observation in other directions.

When substances are met with which refuse absolutely to crystallise, it is necessary to start from pure materials in making them, and to use whatever means are available for purification. Such methods were used by Herth (M. f. Ch. **1**, 89; see also Ber. **25**, 931) in the synthesis of biguanid.

From what has been said, it is evident that workers in the field of organic chemistry have to use a great amount of patience and ingenuity in obtaining new preparations in crystalline form. It must be admitted that chemists are able to work confidently with organic substances only when these are volatile without decomposition, or can be obtained either immediately, or after change into a closely related derivative (see below), in crystalline form. Careful fractional precipitation (see also *A. Path. Pharm.* **20**, 351) may be mentioned as a third method. It is on account of this poverty of methods that the chemistry of organised products (albuminous matters, etc.) is still in its infancy. No general methods whatever are known by which such bodies can be obtained in a pure state, or can be proved to be chemically simple substances when they have been obtained.

Berzelius (*Lehrbuch der Chemie*, Vol. 4, Pt. 1, p. 671) makes the same complaint, and it cannot be said that since his time any important or widely applicable improvement has been introduced. He says in this connection: "One of the most difficult tasks of organic chemistry is to gain a knowledge of the nature of the change when a substance in solution in water passes gradually into several substances having the same property, without the use of any reagent or the appearance of gaseous or solid products. In such cases it is only by chance that the chemist finds means to separate the new bodies from each other and from the original material."

The study of recent literature forces from us the question, why so many students of the science, leaving of course the workers in colour-chemistry and in the synthesis of alkaloids out of account, regard themselves as in duty bound to study the products of the distillation of coal, the relics of a long extinct organic world, and their derivatives, instead of turning their attention to the living forms which surround them. To invent new methods and to follow their application in this region would surely not be less interesting than the piling up of many-membered rings. As an example of what might be done Schmiedeberg's (*A. Path. Pharm.* **28**, 355) recent magnificent work on cartilage may be mentioned. Even from a purely analytical point of view there is much to be accomplished in this department of chemistry.

4. The Transformation of Substances into Closely Allied Derivatives.—This subject has been mentioned already, and must now be treated more fully. The conversion of non-crystalline com-

pounds into such as are crystalline or volatile without decomposition being of the greatest interest, methods of pretty general applicability have been worked out for these purposes.

Basic liquids are converted into their salts, or into platinum, gold, or mercury (Ann. **247**, 5) double salts, which can then be purified; acid liquids yield derivatives in similar ways.

The case with which the hydrogen of a hydroxyl group can be replaced by radicals, is often used to obtain crystalline derivatives which will afford definite information about the constitution of the original substance. Acids are even converted into esters. Crude bilianic acid (Ber. **20**, 1,982) can only be purified by conversion into the di-ethyl ester, an easily crystallisable substance, from which the acid itself can finally be got in solid form. Most frequently the suggested interaction is carried out with substances containing alcoholic hydroxyl groups, and with amines. If the carboxyl group is also present, it is usually desirable to convert that into an ester, say the ethyl ester.

The hydrogen atoms of the hydroxyl, or the amine or amido groups are replaced by the radicals *Acetyl*, *Benzoyl*, *Benzo-sulphonyl*, or *Formyl*.

The best method of *Acetylisng* is that given by Liebermann (Ber. **11**, 1,619). The substance is heated for a considerable length of time with acetic anhydride and dry (fused) sodium acetate in a vessel attached to an inverted condenser. Even very unstable substances can be converted into derivatives which resist exposure to the air. Thus Liebermann (Ber. **24**, 4,130) succeeded in obtaining the acetyl derivative of indigo-white in crystals which were stable in the air, by conducting the reduction of the indigo and the acetylisng at the same time. He mixed one part of the substance to be reduced with two parts of sodium acetate and three parts of zinc dust, and boiled the whole with from ten to fifteen parts of acetic anhydride. Nietzki (B. **16**, 468) used a similar method in preparing diacetyl-safranin hydrochloride. As the free base is difficult to obtain, he mixed the hydrochloride with sodium acetate and boiled it with excess of acetic anhydride.

If reduction is carried out after acetylisng, very unstable substances may be obtained in spite of the presence of the acetyl radical. The reduction product which Baeyer (Ber. **12**, 1,309, obtained from acetyl-isatin with acetic acid and zinc dust is reconverted into acetyl-isatin by the action of the air.

By heating pyrogallol-benzoin (5 gr.) with acetic anhydride (12 gr.),

and fused sodium acetate (10 gr.) in a paraffin bath at 120° for two hours, using an inverted condenser, and then treating with water and recrystallising from alcohol, Döbner and Förster (Ann. **257**, 63) obtained a tetra-acetyl compound of the formula, $C_{38}H_{20}O_{11}(C_2H_3O)_4$. In suitable substances many more acetyl groups may be introduced by the help of condensing agents (see Chap. XII.) which act more strongly than sodium acetate.

It should be said that acetyl chloride and acetic anhydride are able to produce acetylation even when used by themselves. The number of the acetyl groups which enter the compound is of course dependent on the method employed. Erwig and Königs (Ber. **22**, 1,457) report that if quinic acid is boiled with seven parts of acetic anhydride, triacetyl-quinid is the chief product. If the latter, or even quinic acid itself, is heated with acetic anhydride to 240° in a sealed tube, an isomeric triacetyl-quinid is formed. By Liebermann's method the first mentioned isomer is formed. If a grain of fused zinc chloride is added to the acetic anhydride, then tetra-acetyl-quinid is formed in almost quantitative amount. Finally, according to Hesse (Ann. **200**, 233), if quinic acid and the anhydride are heated in a sealed tube at 170° for ten hours, a mixture of the tri- and tetra-acetyl derivatives is obtained.

Bischoff (Ber. **24**, 2,007) found that acetyl-malanile was formed when malanile was dissolved in benzene and boiled with an equi-molecular proportion of acetyl chloride; Kiliani (Ber. **24**, 342) states that digitogenin gives a monoacetyl derivative when treated by Liebermann's method. He found that sulphuric acid could take the place of the sodium acetate yielding the same substance, while zinc chloride gave amorphous products.

The number of acetyl groups which has entered the molecule is sometimes hard to determine, as mono-, di-, and tri-substitution products have a very similar percentage composition if the molecule is large. It is usually preferable to saponify the acetylated substance, and estimate the acetic acid. This is frequently done by adding phosphoric acid, distilling, and titrating the distillate. This reagent is preferred to sulphuric acid, as the latter may give rise to sulphurous acid.

The radical of *formic acid* may be introduced in a similar way to that of acetic acid. Fischer and Hepp (Ber. **23**, 842) made diformyl-diamidophenazine by boiling the base with concentrated formic acid and dry sodium formate.

The radical *benzoyl* was first used by Schotten (Ber. **17**, 2,545), in order to obtain a crystalline derivative of piperidine. He prepared benzoyl-piperidine by the use of benzoyl chloride with sufficient sodium hydroxide to neutralise the hydrochloric acid formed.

Baumann (Ber. **19**, 3,219) worked out the method systematically, and the following example shows how it may be applied. Grape sugar (5 gr.) is dissolved in water (15 cc.) and a 10 per cent. solution of sodium hydroxide (210 cc.) and the necessary benzoyl chloride (30 cc.) are added. After the whole has been shaken until the odour of benzoyl chloride has disappeared, 13 grains of an ester, chiefly the tetra-benzoyl derivative of grape sugar, is found to have been formed.

Pechmann (Ber. **25**, 1,045) dissolved aceto-acetic ether (20 gr.) in water (30 cc.) and a 15 per cent. solution of sodium hydroxide (35 cc.), and shook the mixture up seven times with as many quantities of benzoyl chloride (10 gr.) and caustic soda (30 cc.), continuing the shaking each time until the odour of the benzoyl chloride had disappeared. The mixture was kept cool with water so that the temperature did not exceed 25° at any time during the hour or so which the experiment occupied. The product consisted of equal parts of benzoyl- and dibenzoyl-acetoacetic ether.

In the case of glycerol, Diez (Z. physiolog. Ch. **11**, 472) states that where the solution contains less than 2 per cent., the yield of benzoate by this method is so good that it can be used for quantitative estimation.

For the complete conversion of carbohydrates into the benzoic ester Panormow (Ber. **24**, R. 971) states that stronger caustic soda than Baumann used is necessary. By using 6 parts of benzoyl chloride and 48 parts of 18-20 per cent. caustic soda for every part of the carbohydrate or alcohol he obtained pentabenzoyldextrose, dibenzoylglycogen, and hexabenzoylmannite.

Victor Meyer (Ber. **24**, 4,251) has drawn attention to the fact that ordinary benzoyl chloride often contains chloro-benzoyl chloride, which may lead to the formation of chloro-derivatives. He mentions also elsewhere (Ber. **25**, 209) that it sometimes contains benzaldehyde, which has a disturbing influence owing to the ease with which it acts chemically.

Benzoic anhydride was used by Keller (Ber. **24**, 2,502) for the purpose of introducing benzoyl groups into phenyl-*o*-phenylene-guanidine. He heated the latter for an hour and a half to 130-140° with five times its weight of the anhydride. After extraction with soda solution, a product remained which was found to be the dibenzoyl derivative, $C_{13}H_9N_3(C_7H_5O)_2$.

Benzosulphonyl chloride, $C_6H_5SO_2Cl$, was first applied by Hinsberg (Ber. **23**, 2,962). Schotten and Schlömann (Ber. **24**, 3,689) prepared benzosulphonylpiperidine, $C_6H_{10}N.SO_2C_6H_5$, by the action of benzosulphonyl chloride on piperidine in presence of an alkali in aqueous solution. The yield of this product, which distils unchanged, was 90 per cent. of the theoretical.

Picric acid, di- and trinitrochlorobenzene, and other substances frequently give excellently crystallising compounds with hydrocarbons having a ring structure. Naphthalene yields a picric acid compound melting at 149° (Jahresb. **1857**, 456), a dinitrochlorobenzene derivative melting at 78° (Ber. **11**, 603), and a trinitrochlorobenzene derivative melting at 96° (Ber. **8**, 378).

5. Crystallographic Examination.—The crystallographic characteristics frequently afford means of identifying substances¹ independent of analysis. Indeed since substances with the same empirical formula give the same numbers on combustion, the crystallographic investigation affords the best means of distinguishing isomeric and other bodies related in this way. Crystals selected for examination should not be large merely for convenience in attaching to the goniometer. Good reflecting surfaces and sharp angles are absolutely necessary, and are more usually found in small crystals.

6. Dialysis.—This process was discovered by Graham (J. Ch. Soc. **3**, 6 and 257), and may be used for separating crystalline substances from non-crystalline ones like resins and albumens. The method has received but little attention however. Where it is desired to separate such a mixture, the substance is placed in a tube, the bottom of which is made of a piece of parchment or bladder held firmly in position with twine. This tube, the dialyser, is then suspended in a larger outer vessel containing a suitable liquid. The crystalline substance will be found to have passed almost entirely into the outer liquid after the lapse of a short time, especially if the amount of the latter liquid is large. To facilitate the diffusion the membrane should have a large area and

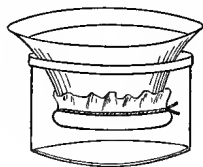


FIG. 1.

¹ A condensed but very excellent account of the methods which may be used will be found in Dr. O. Lehmann's "Die Krystallanalyse," 82 pp., Leipzig, 1891 (Tr.).

the heavier liquid should be placed in the dialyser. The dialyser should hang in the outer liquid, usually water, so that the membrane is not pressed inwards.

Neumeister's method of obtaining pseudo-peptone (*Z. Bio.* **27**, 372) may serve as an example of the use of dialysis. The white of several hens' eggs was slightly acidulated with acetic acid and boiled until coagulation was complete. The filtrate was saturated with ammonium sulphate, and the precipitate which this treatment produced was placed on a filter and washed with saturated ammonium sulphate solution. The precipitate was found to be almost completely soluble in water, and by dialysis the ammonium sulphate was entirely removed in the course of a few days, without an appreciable amount of the substance sought being lost by diffusion. The solution was evaporated on the water bath and gradually deposited a glassy material. From the mother-liquor a jelly was precipitated by alcohol which showed properties with the usual reagents similar to the glassy deposit. On account of its relation to peptone it received the name pseudo-peptone.

Instead of water various organic liquids may be used. Graham obtained for example solutions of silicic acid in alcohol, ether, and carbon disulphide. Schneider (*Ber.* **25**, 1,166) even made an alcoholic solution of colloidal silver.

Warming and frequent gentle shaking promote the dialysis of water solutions. Since the process becomes slower as the proportion of the diffusible material becomes less, it is advisable, after some time, partially to evaporate the contents of the dialyser, and then submit them afresh to the operation.

CHAPTER III

DECOLOURISING LIQUIDS

1. Charcoal.—The decolourising power of charcoal was first recognised last century by Lowitz. For laboratory use pure blood charcoal is best. According to Skraup (*M. f. Ch.* **1**, 185), charcoal containing iron is to be avoided.

The decolourisation is produced by boiling the liquid with animal charcoal, and the operation has sometimes to be continued for hours (*Ann.* **240**, 169). It must be noted that the charcoal frequently takes up a considerable proportion of the substance which is being purified. According to Liebermann (*Sitzungsberichte d. Wiener Akad.* **1877**, 2, 331), potassium urate is held by it very tenaciously, and the same is true of aromatic acids; and salts of fatty acids are decomposed so that the free acid is found in the filtrate. It has a similar effect on salts of alkaloids, such as acetate of morphine and citrate of caffeine. Such decompositions occur however only in water, and not in absolute alcohol solutions.

Experience teaches that finely divided charcoal, especially from blood, passes through the filter in small quantity, and in this connection an observation of Liebig's on allantoin may be mentioned (*cf. Biog. notice, Ber.* **23**, 819*c*). On this account substances which have come directly from solutions decolourised by charcoal should never be analysed without recrystallisation and filtration. By boiling the charcoal afterwards with alcohol, or other solvent, the most of the material which remained adhering to it may be recovered.

Heintz (*Ar. Pharm.* **1876**, 390) states that when charcoal has no effect, terra alba is frequently of use.

2. Extraction of Bitter Principles with Charcoal.—Many substances are so strongly held by charcoal that they can even be extracted by its means. Hopff was the first to discover that wood and animal charcoal have the power of extracting bitter principles from infusions of plants, if not in the cold at all events on boiling. According to Kromayer,¹ bone charcoal is the most active form of the substances for this purpose, and is best applied in the granular state, as this is the only one which permits of easy and rapid washing. The use of powdered charcoal leads to many difficulties. For the removal of any ammoniacal compounds which may be contained in it, it must be subjected first to prolonged boiling with water, and then be freshly ignited before use.

Thoms (Ar. Pharm. 1886, 486) extracted in this way 29 grams of a bitter principle from 300 grams of calamus root. Geuther boiled the infusion of this root with animal charcoal until the taste showed that everything of a bitter nature had been taken out of the solution. He then dried the charcoal and extracted the bitter material from it by boiling with absolute alcohol.

3. Sulphurous Acid.—Besides charcoal, sulphurous acid is used for decolourising. Knorr (Ber. 17, 549) employed this agent for removing the colouring matter from 1-phenyl-2-3-dimethyl-5-pyrazolon (antipyrine). A few drops of a solution of potassium permanganate have a powerful effect in the same direction with many fluids.

4. Precipitation.—When a sufficient amount of lead acetate is used almost all colouring matters are precipitated. In general a solution of the neutral or basic acetate of lead is added to the neutral or alkaline aqueous or alcoholic solution of the substance until the filtrate is colourless. For use with alcoholic solutions, basic lead acetate is dissolved in five or six times its weight of alcoholic ammonia. When the filtrate has become as colourless as is attainable by this means, the lead is precipitated with hydrogen sulphide or sulphuric acid. It frequently happens that the precipitate of lead sulphide carries down any remaining colouring matter (Ber. 24, 4,216).

It must not be forgotten that basic lead acetate precipitates, besides colouring matters, many other indifferent substances. All glucosides, for example, come under this head. According to Schmiedeberg (Z. physiolog. Ch. 3, 114), gum and bassorin are usually thrown down by neutral acetate of lead and always by the

¹ "Die Bitterstoffe," Erlangen, 1861, p. 18.

basic salt. The soluble carbohydrates are neither precipitated by the one nor by the other ; the addition of ammonia is required to cause the deposit of their lead compounds. These relations may be somewhat disturbed however by the presence of other substances along with the sugar. Brücke (*Ar. Pharm.* **1880**, 447) has shown that, although lead acetate gives no precipitate in pure glucose solution, it may cause a slight partial precipitation from artificial or pathological urines containing sugar.

This is of course of importance in the determination of sugar in urine, which has to be carried out so frequently by means of the polariscope. The specimen has usually to be decolourised after it has been boiled to remove the (laevo-rotatory) albumen. The acetate is added in known quantity so that the dilution it causes may be considered in calculation. There seems to be no good reason why the use of the acetate should not be replaced by shaking with a small quantity of animal charcoal. In this case there would be no dilution to introduce a complication. It is said, however, that even charcoal can retain a little sugar.

In place of the addition of ammonia referred to above, other bases may be used. Fischer (*Ber.* **24**, 4,220), for example, precipitated the lead compound of ribose by adding to the solution an excess of the basic acetate and then enough baryta water to throw down all the lead. By decomposing the thoroughly washed precipitate with sulphuric acid and evaporating the filtrate from the lead sulphate, he obtained ribose almost free from ash.

It is obvious that the treatment of solutions with acetate of lead for the purpose of decolourisation is at the same time applicable to obtaining the substance carried down, and is in this respect to be preferred to the use of charcoal. Indeed many colouring matters can only be prepared by precipitation in this way, and subsequent separation from the lead. Lead acetate, however, is not the only reagent used for extracting substances by this method. Haemato-porphyrine, for example, may be completely precipitated from urine with the acetate, but Salkowski (*Z. physiolog. Ch.* **15**, 286) recommends, as preferable, mixing the urine with equal parts of baryta water and a ten per cent. solution of barium chloride. The advantage in this case is that the substance sought may be extracted in a pure condition from the precipitate by alcohol acidified with hydrochloric acid.

CHAPTER IV

DISTILLATION

1. Ordinary Distillation.—The object of distillation is the separation of volatile from non-volatile bodies, while fractional distillation is used for obtaining pure chemical substances by carrying out the process systematically under definitely arranged conditions.¹

The liquids to be distilled are heated in glass or metal retorts, or flasks, and Liebig's condensers are usually employed in the

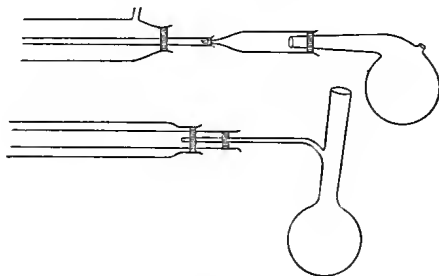


FIG. 2

laboratory for condensing the products which pass over during the operation.

To prevent prolonged contact of the vapours with corks or

¹ The special precautions which the preparation of pure distilled water demands are described in Stas' "Untersuchungen ueber die chemische Proportionen, etc." Trans. by Aronstein, Leipzig, 1867, p. 110. Cf. Ber 24, 1,492.

rubber connections, adapters are used for joining retorts to condensers.

In the case of flasks, a tube sealed into the side of the neck passes through a cork, and so conducts the vapour into the condenser. This tube should take an upward direction for a very short distance, before descending for convenient adjustment to the condenser. If the connection between the flask and condenser is established by means of a suitably bent tube passing through the cork of the former, the end of the tube inside the flask should be ground to a point (Fig. 3), so that the drops collecting in the tube may not be carried over, and a hole should be filed just above the end to permit the unobstructed passage of the vapour.

In order that the connecting parts of retorts or flasks may easily enter the condenser, the inner tube of the latter should be rather wide. On the other hand, the narrower this tube is the more perfect the condensation. To meet this difficulty, several methods have been devised. A narrow tube may have a wider part fused on at the top, long enough to permit of union with retorts and flasks in the ordinary way. Or a piece of somewhat narrower tubing sealed at both ends may be placed inside the inner tube. To prevent its slipping out the latter may be narrowed at a suitable point, while small knobs will prevent the former from resting on the inner tube for its whole length. Ether may be distilled without loss through a short condenser provided with this arrangement, when without it most of the vapour would pass through uncondensed.

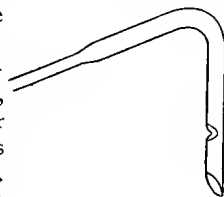


FIG. 3.

Noyes has suggested the use of still another arrangement. He inserts a narrow glass tube, twice as long as the condenser and bent sharply back upon itself in the middle, into the inner tube. The free ends of the tube are bent at an angle of 45° . The same stream of water circulates first through this interior tube and then through the jacket of the condenser. This not only diminishes the section of the inner tube but greatly increases the condensing surface.

In almost all distillations it is necessary to know the temperature of the vapour above the liquid, and all statements of boiling-points refer to this, unless it is expressly mentioned that the temperature has been determined in some other way. The thermometer is

therefore fixed in position so that the bulb is a few centimetres above the boiling liquid.

Many liquids have a tendency to "bump" violently while boiling. Producing a slow evolution of gas in them is the best means of rendering the boiling steady. If the materials being used will suffer it without harm, a little sodium amalgam is added to acid solutions (A. Path. Pharm. **7**, 57), and to alkaline ones a little zinc. If these cannot be employed, platinum clippings, pieces of porcelain, capillary tubes, glass beads, or talc may be used. Kelbe (Ber. **13**, 1,401) recommends a piece of pumice stone weighted with platinum wire as an infallible remedy.

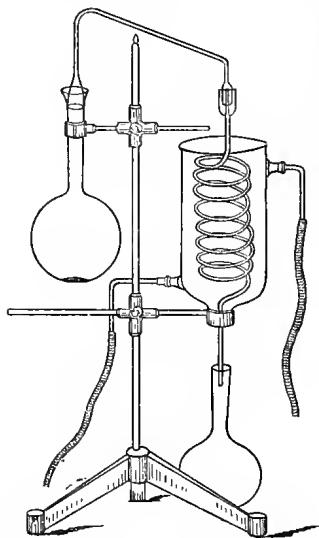


FIG. 4.

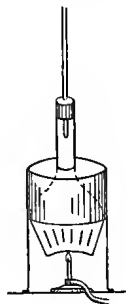


FIG. 5.

The most certain method seems to be that suggested by Bischoff and Hjelt (Ber. **21**, 2,094). The flask, which should be a round bottomed one, is placed in a Babo's funnel. A cylindrical box of sheet asbestos is inverted over the flask so that the neck projects from a hole in the bottom, and the box is in contact with the sides all round (Fig. 5).

Kunz prevents the frothing¹ over of liquids during distillation

¹ It is worth noticing that large quantities of froth, from whatever cause arising, may be at once dissipated in cold liquids by pouring a little ether on the surface.

in quite a different manner by adding some paraffin. The paraffin forms a ring one or two centimetres wide at the surface of the liquid and in contact with the sides of the flask. The liquid is said to boil in the centre with perfect regularity. When a liquid deposits solid matter while boiling, this may be prevented from adhering to the bottom of the flask, and so causing irregular boiling, by the passage of a rapid stream of gas through the liquid. Frequently also liquids which "bump" violently when heated with the naked flame, may be distilled quietly when a suitable bath is used.

2. Thermometers and their Use.—In the determination of boiling-points it is desirable, whenever possible, to have the stem of the thermometer up to the top of the mercury column immersed in the vapour, and for this purpose the flask must have the side tube inserted in the neck at a sufficient height. This cannot always be done, however, and consequently, to allow for the part of the column projecting above the vapour, a correction has to be applied.

According to Kopp (Ann. **94**, 263), the *correction* is applied in the following manner:—The temperature is read off on the thermometer projecting from the apparatus. Another thermometer is held by means of a clamp, so that its bulb is close to the stem of the first and on a level with the middle of the projecting part of its mercury column. A horizontal screen protects the air round the thermometers from being heated by the flame. The corrected temperature is equal to $T + N(T - t) \times 0.000154$, where T is the apparent boiling temperature, t the reading on the second thermometer, and N is the length of the projecting mercury column from the middle of the cork up to T .

The boiling-point depends also on the pressure of the atmosphere. Landolt (Ann. Suppl. **6**, 175) states that, for pressures not far from the normal, it is depressed 0.43° for each decrease of 1 mm. in the pressure. It is usual at present to give the pressure at which the boiling-point was determined, instead of following the really preferable plan of correcting the observed boiling-point and giving it with reference to normal pressure.

Städel and Hahn (Ann. **195**, 218) have devised an apparatus which permits distillations and boiling-point determinations to be carried out under any desired pressure. The apparatus need not, however, be described, as these operations are seldom conducted

under abnormal conditions except in the single case of distillation in almost complete vacuum, which will be considered later. Some attacks (Ber. **13**, 839) to which the apparatus has been subjected have been successfully repelled by the authors. Improvements have been suggested by Schumann (Pogg. Ann. **212**, 44).

In connection with the *choice of a thermometer* some points are worthy of notice. Zincke (Ann. **161**, 95) suggested that it should be so constructed that the mercury column was only a short distance above the bulb when it stood at 100° . In this way the stem might be made shorter than in the common form and the instrument much handier. Gräbe (Ann. **238**, 320) then suggested that thermometers should be made so that the whole, or practically the whole, of the mercury could be immersed in the vapour.

By the use of such instruments it is possible to obtain corrected boiling- or melting-points with any thermometer after its readings have been compared with those of four short standard thermometers. The latter are constructed so that the first only goes up to 100° , the second begins at 100° , the third at $216-218^{\circ}$ (b.-p. of naphthalene), and the fourth at $304-306^{\circ}$ (b.-p. of benzophenone). The comparison must be carried out under as nearly as possible similar conditions.

Anschütz¹ states that for still greater accuracy the whole scale may be divided among seven thermometers whose degrees are divided into fifths. The smaller number of degrees on each thermometer still permits the whole column to be immersed in the vapour.

Thermometers, filled under pressure with nitrogen, reading as high as 460° (Ann. **259**, 106, and **264**, 124), are manufactured by Geissler, while Schweitzer (Ann. **264**, 194) speaks of one made by Gerhardt whose scale almost reached 500° . In the case of the last, however, comparison with an air thermometer showed that a correction of 29° was necessary above 400° . For higher temperatures Meyer and Goldschmidt (Ber. **15**, 141) suggest a form of air thermometer which is well suited for chemical work.

The new electric thermometers are now most convenient for measuring high temperatures. They are especially applicable in the case of explosives, as the scale on which the temperature is read off may be placed at any distance.

Breakage of the stem is very apt to occur in inserting thermometers into corks and rubber stoppers or in withdrawing them

¹ "Destillation unter vermindertem Druck," Bonn, 1887, p. 16.

again. To avoid this the following arrangement may be used :—A short piece of tubing, *ab* (Fig. 6), just wide enough for the passage of the thermometer is fitted into the cork.

On the outer end of this is slipped a piece of rubber tubing, *c*, which holds the thermometer firmly when it is in position. In this way the thermometer can be easily inserted after the apparatus has been put together, and removed when the distillation is over. If the apparatus is a complicated one and leaks slightly in one or two places, a gentle stream of air can be drawn through the whole by a pump, and so any escape of vapours may be prevented.

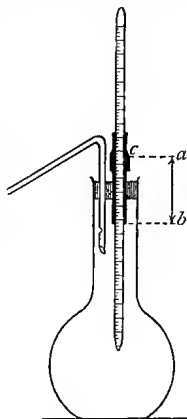


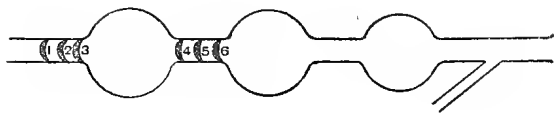
FIG. 6.

3. Fractional Distillation.—In the fractional distillation of a mixture the distillate is collected in separate portions, each of which has come over within narrow limits of temperature. By repeating the process several times one or more products are finally obtained during whose distillation the mercury column has hardly moved perceptibly. The results are then, except in a very few exceptional cases, pure chemical substances.

This operation is greatly assisted by the use of certain pieces of apparatus which closely resemble in principle the towers used by manufacturing establishments. Sometimes the separation can be effected in no other way (Ber. **22**, 607).

Under the direction of Victor Meyer, Kreis (Ann. **224**, 268) submitted the various forms of the apparatus to a test of their efficiency, and obtained the following results :—

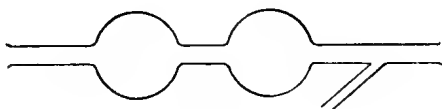
(1) For substances which boil in the neighbourhood of 100° the Linnemann tube (Ann. **160**, 195), containing little wire gauze trays of platinum, and the Hempel tube (Z. analyt. Ch. **20**, 502) are found to be the most effective. The Le Bel-Henninger apparatus (Ber. **7**, 1,084), which only differs from Linnemann's in having side tubes to let the liquid flow easily back into the flask, is declared to be too complicated and not in the least better than the plain apparatus. It is said to be no disadvantage that the boiling has to be frequently interrupted on account of the platinum gauze cups becoming filled with the liquid. The frequent stoppage of the distillation gives the



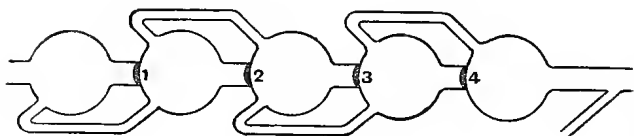
LINNEMANN.



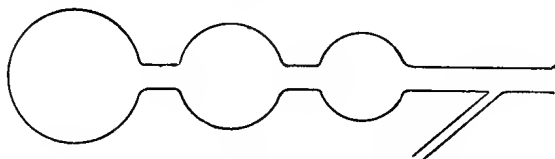
HEMPEL.



WURTZ.



LE BEL-HENNINGER



FLASK WITH BULBED NECK.

FIG 7.

lower boiling constituent time to volatilise, and so facilitates the separation. Hempel's apparatus consists of a glass tube filled with beads, and may perhaps be preferred to Linnemann's apparatus, because it consists entirely of glass and is very easily made.

By the use of these devices as good a separation may be attained with one distillation as with twelve distillations from an ordinary flask.

(2) By the use of Wurtz's bulb tube (Ann. **93**, 108), as good a result is obtained with six distillations as with twelve from an ordinary flask without its intervention. The efficiency of Wurtz's apparatus is not increased if four bulbs instead of two are used, nor when the tube is made of the full width of the bulbs all the way up.

(3) Even for substances boiling at a high temperature the result is appreciably better when a bulb tube is added than when a long-necked flask is substituted for one of the ordinary pattern.

When the quantity of the substance is small, or when the vapour has a tendency to attack cork or rubber, Hantzsch (Ann. **249**, 57) recommends the use of a flask with a long and wide neck, which can be filled with beads. To prevent the latter falling into the flask a piece of platinum or nickel wire gauze is placed at the base of the neck. Frequent references in the literature show that in general flasks having somewhat lengthened bulbed necks are to be preferred to ordinary flasks with bulb tubes attached above.

Winssinger (Ber. **16**, 2,642) suggests an excellent way of separating the constituents of the vapour during fractionation (Fig. 8). Through the neck of the flask he passes a tube, closed at the bottom, in which a very slow stream of water or mercury circulates, whose speed is controlled by a stopcock. Water is used for substances boiling below 100° , mercury when the boiling point is higher. The smallest alteration in the speed of the stream produces instantly a rise or fall in the column of mercury in the thermometer. By proper regulation a definite temperature, suitable for the separation of the vapours, may be maintained with great exactness. Claudon (Bull.

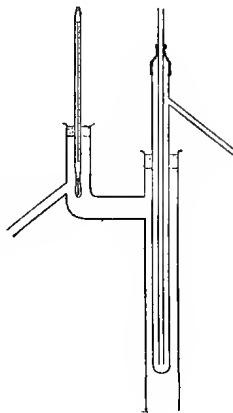


FIG. 8.

Ch. 42, 613) states that the efficiency of the apparatus is greatly increased by surrounding the inner tube with wire gauze and sheltering the whole apparatus from draughts.

When distillation in a stream of hydrogen, carbon dioxide, or other gas is to be carried out, Hoffmann (Ber. 6, 293) recommends the use of a flask like that in the figure (Fig. 9).

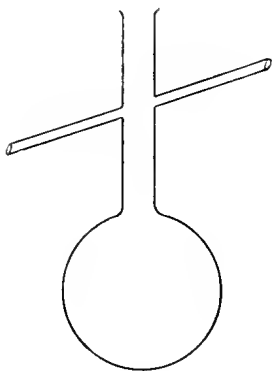


FIG. 9.

4. The Condenser.—If it is desired to heat a liquid which is all or partly volatile, the flask or retort containing the liquid is attached to a condenser in such a way that the condensed material must always flow back into the flask. If a higher pressure than that of the atmosphere is required during the boiling, the upper end

of the condenser is connected with a glass tube which is bent downwards and dips into a vessel of mercury. If the question is to ascertain whether gases issue from the condenser during the process, a Liebig's bulb apparatus, filled with a suitable solution, is attached to the open end. On the other hand it is often requisite to permit water, formed by the chemical action, to escape in spite of the condenser. Ephraim (Ber. 24, 1,027) attained this by using a simple tube surrounded by a coil of lead tubing through which steam was passed. Gabriel (Ber. 18, 3,470) even bent the upper end of the tube over and followed the course of the reaction by measuring the amount of the water which came off. In a precisely similar manner Bischoff (Ber. 21, 2,093) secured the removal of an easily volatile alcohol produced by the saponification of an ester of high boiling point.

If a solid condenses in the tube and threatens to stop it up, a suitable volatile solvent is poured in. For example, Gottschalk (Ber. 20, 3,287) found that in oxidising pentamethylbenzene with nitric acid, the hydrocarbon volatilised, and had to be washed back into the flask with benzene.

If a gas is generated during the boiling, or a stream of gas is led through the contents of the flask, it will be found that, in spite of the most thorough

cooling, an amount of the vapour corresponding to the vapour tension of the liquid will be carried off with the gas. The greater part of this may be caught by leading the gas, after it leaves the condenser, through a vessel of water. If, for example, in order to make carbon tetrachloride, chlorine is led through chloroform in sunlight and the gas escaping from the condenser is passed into water, a heavy liquid, consisting of a mixture of chloroform and carbon tetrachloride, will soon collect at the bottom of the vessel. Where the liquid does not attack metals, the Liebig's condenser, which is

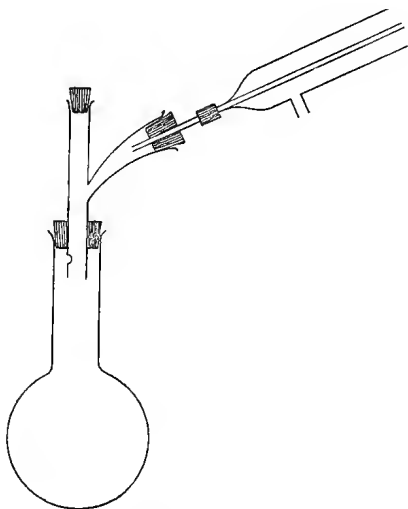


FIG. 10.

somewhat unhandy on account of its length, may be conveniently replaced by Soxhlet's bulb condenser.

Volhardt (Ann. **253**, 207) recommends that when retorts have to be heated rather strongly for long periods in connection with inverted condensers, they should be made of potash glass, and that, reviving an old custom, the part within reach of the flame should be covered with a thin layer of clay and sand. He was able to keep such protected retorts in use for weeks, while naked glass, especially soda glass, seldom stood more than one operation.

Otto¹ suggests that lean clay should be ground up to a fine paste with water containing a little soda, and this mixture should be painted on with a brush. When the first coat is dry a second is added, and this treatment is usually sufficient even if the layer is not thicker than a visiting card. If the whole retort is painted over, two bare places are left opposite to each other for observing changes going on in the interior. Winkler (Ber. **24**, 1,971) stirs up three parts of finely powdered firebrick and one part of common clay with ordinary water glass solution, and applies this paste to the surface of the glass. The coating is repeated two or three times and each layer is dried on the sand bath.

5. Distillation in a Current of Steam.—A current of steam is frequently used for volatilising substances which cannot be distilled alone or can only be distilled with decomposition. This treatment is often the best way of separating one body from the other components of a mixture.

The operation consists in passing a stream of water vapour through the liquid while the latter is itself heated on a water or sand bath. The steam is best made in a metallic boiler. In the absence of such a vessel, a flask holding two or three litres may be substituted. It is filled half full of water and a few drops of sulphuric acid and several pieces of zinc are added. The slow evolution of hydrogen prevents irregular boiling, and so a steady stream of vapour may be maintained for hours in succession.

When substances which are easily coloured by oxidation, like aromatic amido-compounds, are to be driven over with steam, it may be necessary to work in a current of carbon dioxide, or following Bechhold's suggestion (Ber. **22**, 2,378), to saturate the water in the boiler with hydrogen sulphide before starting the experiment. Schultz (Ber. **20**, 2,721) states that colourless products may be secured by adding animal charcoal to the liquid to be distilled.

If the substance passes over very slowly with a current of ordinary steam, or even fails to pass over at all, the desired result may often be attained by using superheated steam. The superheating is produced by leading the steam through a coil of copper tubing (Fig. 11), containing about ten turns, and heated by a quadruple Bunsen burner. The tube should have a bore of about 5 mm., the thickness of the wall should be 1.5 mm., and the internal diameter of the spiral about 3 cm. The extremity next to the flask may conveniently be brazed into a wider tube in which a cork can be

¹ Graham-Otto, "Lehrbuch d. Chemie" [4], pp. 127, 385.

inserted. The connections must be made with corks, as rubber stoppers will not stand such temperatures for many minutes. If corks also fail, soapstone, or some similar material, may be used.

Attention need be paid to the extent of the superheating in the case of very sensitive substances only. Salkowski (*Z. physiolog. Ch.* **9**, 493) says that in driving over skatole carboxylic acid, when obtained as a product of decay, in this way, a large part is resinised if the steam is heated too much.

The glass tube conducting the steam into the distilling liquid is bent

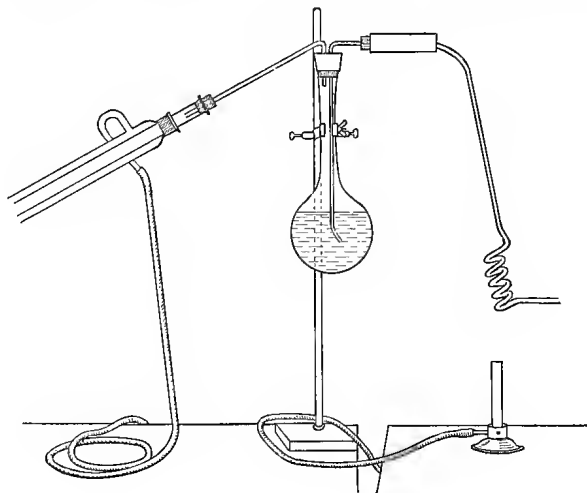


FIG. II.

slightly at the point and is usually made of hard glass. Both kinds of glass become brittle after repeated use, but hard glass is less liable to crack accidentally. It is unnecessary in this case to heat the liquid, as the steam keeps it up to its natural boiling-point. This may be raised, however, by judicious addition of some indifferent salt.

Rasinski (*J. pr. Ch.* **137**, 39) made experiments on fractional distillation with steam, but the results with petroleum hydrocarbons were unfavourable. After Naumann had proved that liquids which do not mix with water must be carried over by steam at temperatures below the boiling-point of water, Lazarus (*Ber.* **18**, 577) took

the matter up again. He distilled the mixtures in a stream of steam of moderate speed, and caught the distillate in two or three portions. From a mixture of 25 cc. toluene and 25 cc. nitrobenzene he obtained—

Fraction.	Temp.	Vol.	Content.	
			Toluene.	Nitrobenzene.
1	90–95°	21 cc.	19 cc.	—
2	95–98°	6 cc.	3·5 cc.	—
3	98°	23 cc.	—	23 cc.

He thus recovered 22·5 cc. of toluene and 23 cc. of nitrobenzene. Benzene and toluene could not be separated sharply by this method, so that it seems to apply only to cases where the boiling-points are sufficiently far apart.

The vapours of alcohol, ether, and perhaps other substances, may likewise be used for separating mixtures. Bunzel (Ber. **22**, 1,053) found that distillation with alcohol vapour was the best method for obtaining pure α -pipecoline, while Askenasy and Victor Meyer (Ber. **25**, 1,702) obtained perfectly pure nitropropylene by distilling in a stream of ether vapour. Acetylacetone and acetonylacetone are likewise examples of substances volatile with ether. In preparing such substances, where repeated extraction with ether is necessary, the same ether will naturally be used over and over again; that which has been obtained by distillation from the result of one extraction being applied to extracting the next lot, in order that the loss of material may be reduced to a minimum.

6. Dry Distillation.—The dry distillation of organic substances always results in considerable loss by decomposition. It was not until 1830 that anything further was known than that water, tarry oils, and solid residues were formed. It was discovered then that organic substances are broken up into simpler bodies like water, carbon dioxide, carbon monoxide, solid, liquid and gaseous hydrocarbons, and carbon. On the other hand Saussure (Gmelin [**4**], **4**, 552) showed that leading alcohol or ether vapour through red-hot tubes produced naphthalene.

In 1832, Liebig and Dumas found that water, carbon dioxide, and acetone were formed by distilling acetates, and Persoz (Ann. **33**, 181) discovered the formation of carbon dioxide and methane by decomposing the same salts under other conditions. After Mitscherlich (Ann. **9**, 43) had determined, in 1833, that the dry distillation of benzoates yields equal volumes of benzene and carbon dioxide, both measured as gases, the operation became a common one in all laboratories.

The experiment is usually carried out by distilling the substance in limited quantities from small retorts or bulb tubes, or simply from hard glass tubes heated in a combustion furnace. To prevent the material caking together, it is mixed with sand, fragments of pumice, or other similar substance. Jacobsen's suggestion (Ber. **12**, 429), to add iron filings to the calcium salt or whatever is distilled, is a very valuable one. This overcomes the disadvantages arising from the low conducting power for heat and tendency to cake together which characterise the lime salts. A steady distillation can be accomplished at a relatively low temperature, and the glass vessels can be used repeatedly, as they are much less apt to crack.

Dry distillations are usually very wasteful of time, as good yields can only be obtained by heating a small amount at once; a larger amount must be strongly overheated, in order that the temperature may be high enough in the heart of the mass. The tall shape of the body of the ordinary retort contributes somewhat to this inconvenience.

This difficulty has been met in two ways. The first suggestion was that of ter Meer (Ber. **9**, 844), who used a shallow iron vessel, on which a flat iron top, with a tube to conduct away the vapour, could be clamped. The substance was spread in a thin layer on the floor of the retort.

The first suggestion was

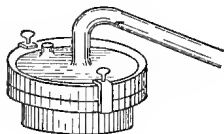


FIG 12.

The advantage of this apparatus may be seen from the fact that Lieben and Rossi (Ann. **158**, 147) obtained 250 grams of the crude aldehyde by distilling a mixture of calcium butyrate and formate in a hundred portions of 10 grams each from small glass retorts. With ter Meer's apparatus twenty lots of 50 grams each yielded 270 grams of the same aldehyde. A better result even than this seems to be obtainable when carbon dioxide gas is led through the apparatus and the vapours are swept out

as soon as they arise, especially if at the same time a constant source of heat, such as a bath of sulphur vapour, is used. Sidney Young (J. Ch. Soc. **59**, 623) describes an apparatus made on this plan by means of which he obtained very nearly the theoretical yield of dibenzylketone from the calcium salt of phenylacetic acid. When no such apparatus is available the yield, with use of small glass retorts, may be much improved by covering them with an adjustable mantle of sheet iron (Mager, Dissert. Leipzig, 1890) to aid in distributing the heat.

The calcium salt is usually thoroughly dried before distillation, although this is more a matter of tradition than a result of any special reasoning. The admixture of dry chalk is said to improve the yield.

It is worth mentioning that the same acid will not always give the same products when heated with different bases. Meyer and Hoffmeyer (Ber. **25**, 2,121) obtained xanthone by distilling hydrofluoric acid with lime; but on applying baryta or soda lime they obtained an entirely different derivative.

In many cases the sodium or potassium salt is to be preferred to the salts of the alkaline earths for some particular purpose. Grosjean (Ber. **25**, 478) mixed two parts of the dry barium salt of undecylenic acid with one part of powdered sodium ethylate, and heated the mixture in a hard glass retort under a diminished pressure of 50 mm. He obtained more than fifty per cent. of the theoretical yield of decylene.

By distilling the sodium salt of *o*-quinoline sulphonic acid with five times its weight of potassium cyanide under diminished pressure, Lellmann and Reusch (Ber. **22**, 1,391) obtained *o*-cyanoquinoline.

Dry silver salts are frequently distilled, and Kachler (M. f. Ch. **12**, 339) even tried to give a general equation for the results of distilling silver salts of fatty acids.

Pechmann (Ann. **264**, 305) found that the silver salt of cumalic acid was not obtainable, and used instead the mercurous salt, which he distilled in a stream of hydrogen, in portions of 20 grams at a time, from tubulated retorts.

7. Distillation in a Vacuum.—The introduction of distillation *in vacuo* was a great advance in the art of distilling, and is now easily carried out. Its convenience lies in the fact that many substances may be distilled under diminished pressure, which would decompose if treated in the ordinary way.

It is somewhat extraordinary that common distilling flasks and retorts, provided that they are not unusually thin, may be used with safety, even when the air is pumped out so as to leave only a few millimetres pressure in the interior. The only limitation is that it is not advisable to use vessels larger than half a litre, as with larger flasks breakage is very common (Ber. **24**, 937). The ordinary glass apparatus may therefore be employed in all cases, provided that baths are used for heating instead of the naked flame. As a precaution against accidents, it is advisable to use a plate of glass or to cover the flask with an asbestos cloth for the protection of the experimenter.

The only disadvantage to which this operation is exposed, is that the liquid is apt to boil irregularly, causing portions to be thrown up into the condenser. Anschütz, in his paper on this subject,¹ points out that Dittmar was the first to show, in a paper published in 1869, how this may be overcome in almost every case. His suggestion was to permit a small but regular stream of dry gas to be drawn through the boiling liquid during the distillation. Flasks may now be bought (Ber. **24**, 597) which have suitable capillary tubes fused in. When these are not obtainable an ordinary distilling flask with side tube is provided with a rubber stopper with two holes. The thermometer passes through one of these, and through the other a tube is inserted which is drawn out into a capillary at the lower end, and reaches almost to the bottom of the flask (Fig. 13). At the upper end a rubber tube and screw clamp are attached. By means of the latter a little air may be admitted, and so regulated that a constant stream of minute bubbles rises through the liquid. When air is unsuitable, carbon dioxide or hydrogen can be used instead. Rubber stoppers are usually employed in fitting up the apparatus in preference to corks, as it is more easily kept air-tight when they are used. Brühl (Ber. **24**, 3,375), however, recommends the use of corks dipped in strong collodion solution, as they are in every way as good for the purpose as rubber stoppers.

According to Hell and Jordanoff (Ber. **24**, 937), it is advisable to fix the tube bearing the capillary with a special clamp, as the heat of the distillation is apt to soften the rubber stopper and permit the tube to be sucked in and its capillary broken. This

¹ "Destillation unter vermindertem Druck im Laboratorium," Bonn, 1887.

precaution may prevent the untimely interruption of a half-completed distillation.

In regard to thermometers the remarks made under the head of ordinary distillation apply equally here.

It is in most cases unnecessary to use a condenser, although the receiver may be cooled with ice, and possibly a simple tube inserted between the flask and receiver.

It sometimes happens that the pressure of the water changes, or that from some other cause the water runs back into the apparatus. To avoid this a Woulff's bottle may be connected

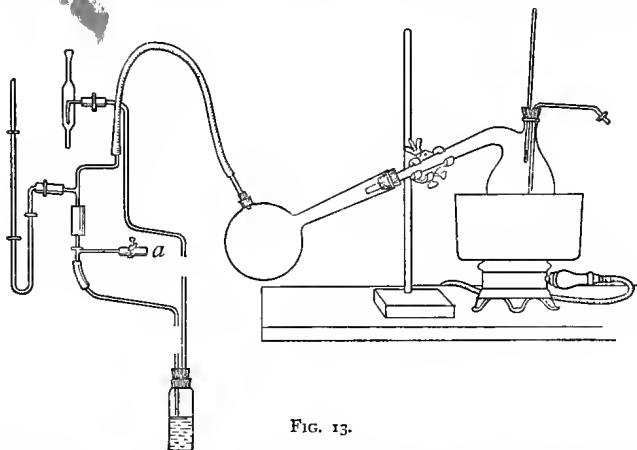


FIG. 13.

between the pump and the apparatus. Better still is the arrangement (Fig. 13) used in the Königsberg laboratory, as it absolutely prevents the possibility of any water passing back.¹ A tube connects the pump with a bottle of mercury. Through the other hole in the stopper of this bottle passes a tube, at least a metre in length, reaching to the bottom of the mercury. The apparatus to be exhausted is connected with the second tube. If the pump ceases entirely, the mercury will rise about 760 mm. in this tube; but, as its length is over a metre, nothing can reach the interior of the apparatus, and the distillation cannot suffer.

¹ This apparatus is manufactured by Max Stuhl, Philippstrasse, 22, Berlin, N.W. The glass tubes are all sealed together in one piece, thus doing away with rubber connections, and the arrangement is mounted on a narrow board.

The pressure in the apparatus is read off by means of a manometer. To avoid breakage of this, if the mercury should be allowed to rise too rapidly and strike the top with violence, it is well to narrow the bore of the tube at a point a little below the top, so that the mercury may have to traverse an almost capillary opening before it can completely fill the tube. A similar precaution may be recommended in the case of the vertical tube. The narrow part should be placed just above the surface of the mercury in the bottle. In the figure *a* is an opening for admitting air after the distillation is at an end.

It is most usual to employ the lowest pressure which the pump can produce, yet there seems to be a difference of opinion as to what reduction of pressure is most serviceable.

Krafft (Ber. **15**, 1,692) states that a pressure of 100 mm. of mercury is the best to use, because, while it is sufficient to protect most substances from decomposition, variations in the pressure produce less effect on the readings of the thermometer than when very low pressures are used. Irregular boiling also requires no special attention, as it rarely appears except at much lower pressures. In order to keep the pressure within 0.5 mm. of that desired, he inserts between the apparatus and the pump a large bottle, which acts as a kind of vacuum reservoir. This bottle may be connected with the air, or with a gas holder filled with hydrogen or carbon dioxide, by a tube closed by a stopcock. After a little practice a stream of gas can be admitted sufficient to keep the mercury in the manometer at any desired level. According to Kahlbaum,¹ on the other hand, the full advantages of distillation in partial vacuum are obtained only when 25 mm. pressure or less is used.

This method of distilling was at first very inconvenient where fractionation was necessary, as the apparatus had to be taken apart every time the receiver was changed. Of all the forms of apparatus which have been invented to simplify the operation, that of Claisen is perhaps the one that best combines absence of complication with efficiency. The more elaborate apparatus of Lothar Meyer (Ber. **20**, 1,834) has also its special advantages.

In Claisen's apparatus (Fig. 14) the condenser is connected with the wide tube *a*. The tube *b* leads to the manometer and pump, either directly or with intervention of the large bottle and mercury valve for preventing back flow of water already

¹ "Siedetemperatur und Druck," Leipzig, 1885, p. 72.

described. By means of the three-way stopcock *c* air may be admitted, either into the whole apparatus, or only into the test tube or flask attached at *d*, which acts as receiver. In this way the receiver, which fits tightly on to a rubber stopper, may be changed as often as may be necessary without causing the level of the manometer to vary appreciably.

If the distillate solidifies quickly an additional inconvenience is added to the others attending this mode of fractionating. The substance will in this case usually collect above the stopcock in Claisen's apparatus. If the part *a* is made wide enough to hold all the distillate, this need not interrupt the distillation until the whole has

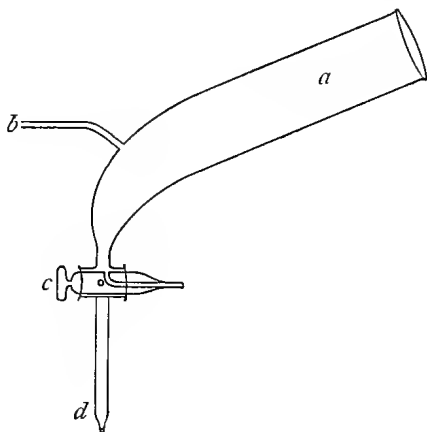


FIG. 14.

passed over. The contents can then be melted out by the cautious application of heat after the apparatus has been taken apart.

Where the moisture passing back into the apparatus from the pump has a disturbing influence, a tube containing phosphorus pentoxide may be inserted between them.

8. Leading Vapours through a Red-hot Tube.—This method is frequently used for preparing aromatic hydrocarbons where milder means do not suffice. If one heating only is desired, the vapours are led through an iron, or if necessary a glass, tube placed

in a combustion furnace. Krämer and Spilker (Ber. **23**, 84) suggest the use of a double tube (Fig. 15). The lower branch is placed in the furnace, the upper heats the vapours preliminary to their

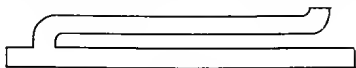
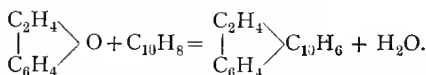


FIG. 15.

entering the lower. For example, although cumarone passes through unchanged at a dull red heat, a mixture of cumarone and naphthalene loses water and forms chrysene.



It is suggested by Lüddens (Ber. **8**, 870) that carbon dioxide may be led through the tube along with the vapours so as to prevent their lingering too long in the passage. By this means he obtains diphenyl from benzene without any great deposition of carbon. At other times it is desirable to expose the vapour repeatedly to the influence of a high temperature if a single exposure is not sufficient. In this case an apparatus may be employed which was originally used by Michaelis (Ann. **181**, 283) for making phosphenyl derivatives. It was adopted later by La Coste and Sorger (Ann. **230**, 5),

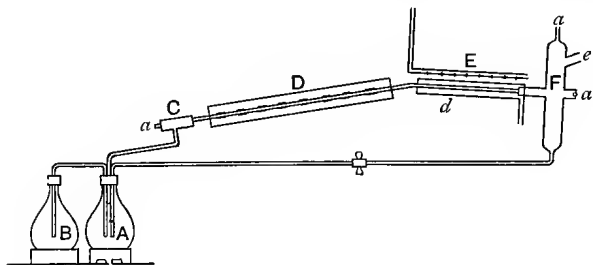


FIG. 16.

who were thus enabled to expose benzene vapour to a bright red heat for weeks in succession.

The benzene or other substance is placed in the flask A (Fig. 16). The adapters C and F and the connecting tubes are made of lead,

The iron tube D is placed in an inclined combustion furnace. After the vapour has been heated it passes through a part of the tube, which is cooled by a spray of water from the tube E. Whatever is still condensible is cooled by a condenser attached at *c*. The cooling by the water from E prevents the melting of the adapter F at its junction with the iron tube. The condensed material flows back to the flask A through the long lead tube. Another tube, passing to the bottom of both, connects the flask A with the safety flask B. The top of the condenser is provided with a descending tube for the purpose of causing any escaping gases to bubble through a vessel of water. The openings *a, a, a*, and the coupling G are provided for convenience in cleaning the apparatus.



FIG. 17.

9. Distillation under Pressure.—No apparatus specially designed for this purpose is in use in the laboratory. Engler made petroleum hydrocarbons on a large scale by distilling fats in an apparatus invented by Krey (Ger. Pat. 37,728) for technical use. In some parallel experiments in the laboratory (Ber. **21**, 1,818), he employed sealed tubes containing each about thirty grams of the substance. They were bent at an obtuse angle and placed in a digester in such a way that the empty limbs of the tubes hung downwards outside. After having been heated for four hours at 350° the tubes were removed, the gases allowed to escape, and the capillaries resealed. This operation was repeated

until the appearance of a sufficiently mobile liquid product indicated that the action was complete. The results were the same as when Krey's apparatus was used.

10. Boiling-Points.—When the boiling-point of a liquid, on account of the small quantity available for examination, cannot be ascertained by distillation, this important constant may be determined by the use of a single drop even of the substance by the method suggested by Siwoloboff (Ber. **19**, 795).

The liquid is placed in a glass tube which has been drawn out and sealed at the bottom. A capillary tube, sealed up at A, is introduced, and the whole is attached to a thermometer and treated as in the determination of a melting-point (Chap. VIII.). Before

the liquid reaches the boiling-point single air bubbles proceed from the small volume of air in the capillary below A ; these become gradually more numerous till an uninterrupted thread of small bells of vapour is established. At this moment the thermometer shows the exact boiling-point of the liquid. The operation should be repeated several times and the mean of the observations taken. The capillary prevents violent boiling, and must be renewed for each experiment.

Main (Ch. News, **35**, 59), Hasselot (Z. analyt. Ch. **18**, 251), and Schleiermacher (Ber. **24**, 944), suggest other forms of apparatus for this determination.

CHAPTER V

DRYING SOLIDS AND LIQUIDS

1. Drying in Desiccators.—Solids may be dried by heating to a sufficiently high temperature in a Lothar Meyer's air bath (Ber. **22**, 879) ; when they will not stand this treatment they are placed in desiccators. The latter are used also for keeping substances which have been dried in the heat, to avoid their attracting moisture again.

As sunlight produces more decomposition than is ordinarily supposed, it is well to have a dark glass bell jar at hand for such cases (Ber. **21**, 2,529).

A variety of drying agents, such as concentrated sulphuric acid, calcium chloride, quicklime, barium oxide, and potassium and sodium hydroxides, are used to charge the desiccator. If the substance has a tendency to lose carbon dioxide or ammonia, it will be dried in an atmosphere of one or other of these gases ; in the latter case moist sal-ammoniac may conveniently be scattered on the pieces of potassium hydroxide.

The relative drying power of various substances has been examined by Müller-Erzbach (Ber. **14**, 1,096). He finds that phosphoric anhydride, concentrated sulphuric acid, and dry potassium hydroxide are almost equal in power ; sodium hydroxide and calcium chloride containing but little water are likewise nearly equivalent in drying capacity. Moist caustic soda, however, is entirely deprived of its water by caustic potash, while the difference in the vapour tension of water over phosphoric anhydride and almost anhydrous calcium chloride is only a fraction of a millimetre of mercury ; sulphuric acid works more rapidly than calcium chloride (Ar. Pharm. **1884**, 107).

Hempel (Ber. **23**, 3,566) drew attention to the fundamental defect

in ordinary non-evacuated desiccators, which consists in the fact that the drying agent is placed at the bottom. Since moist air is lighter than dry air only a slow interchange can take place between the strata of gas in the vessel. He found that in fact a quantity of water which took nine days to evaporate in the ordinary form of desiccator, was absorbed by the drying agent in three, when the only difference between the experiments was that the drying agent was placed above instead of below. He has lately described a convenient form of the apparatus (Z. f. angew. Ch. **1891**, 201) in which he has given effect to this principle.

All drying is much accelerated by using desiccators provided with a tubulus through which the air is withdrawn after the substance has been placed in position. A suitable grease for rendering the adjustment of the ground glass surfaces air-tight may be made by melting together three parts of tallow and one part of white wax.

According to Pflüger (P. Ar. **38**, 311), a good water pump will reduce the pressure in a desiccator to 11 mm. of mercury at 16–20°. If concentrated sulphuric acid is then admitted, the pressure sinks quickly to less than 1 mm., showing that practically all the air has been removed.

Instead of concentrating small quantities of solutions by heat, they may conveniently be allowed to evaporate in a desiccator, a process which is much assisted by placing the apparatus in a warm place, or by evacuating. Desiccators have even been designed in which liquids may be boiled and so evaporated *in vacuo*. Anschütz (Ann. **228**, 305) and Brühl (Ber. **24**, 2,458) have described arrangements for this purpose. The author has found the following easily constructed apparatus very convenient (Fig. 18).

The strong ground-glass plate on which the bell jar rests is bored in the centre and provided with a rubber stopper through which a lead pipe passes. A porcelain dish stands on a tripod above the hole, and its interior surface is covered as completely as possible with coils of the lead pipe; wire can be used to hold these in position. By this means a current of hot water or steam may be led through the pipe and a kind of steam bath produced. For the better distribution of the heat the coils of pipe may be covered with powdered copper, such as is obtained by the reduction of the oxide. Small dishes of sulphuric acid can be placed under the tripod, and the plate is elevated on two pieces of wood to give the space necessary below for the exit of the lead pipe.

The air is withdrawn by a tube passing through the neck of the

bell jar. A second tube provided with a stopcock entering with this, is bent twice at right angles and dips into a beaker. When the stopcock in this tube is opened the liquid is forced in by the pressure of the air, and the basin can therefore be replenished during the evaporation without interrupting the pump. Walter (J. pr. Ch. **32**, 425), to whom we owe the suggestion of the second tube,

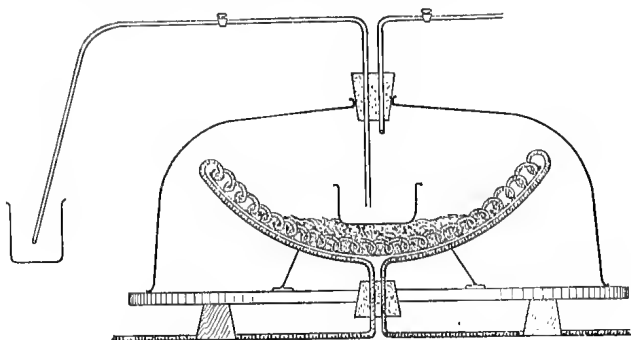


FIG. 18.

has also designed an apparatus for evaporation *in vacuo*, but it is less simple than that described.

It might be more advantageous to connect the pump with the lower part of the bell jar by passing the tube leading from it through the rubber stopper in the plate.

If it is desired to evaporate carbon disulphide, ether, chloroform, or benzene, the desiccator is charged with crude paraffin of low melting-point in place of the usual drying agents. Liebermann (Ber. **12**, 1,294) states that the evaporation goes on very quickly—most rapidly in the case of the first-named solvent, and least so in the case of the last. The paraffin becomes liquid during the process, but does not thereby lose its absorbing power. The solvents may be recovered in a pure condition by distilling the paraffin solution.

Many substances are extremely hard to dry. Schmiedeberg (A. Path. Pharm. **28**, 364) found, for example, that acid chondroitine sulphate and chondroitine itself were decomposed by remaining in a desiccator at 100° either *in vacuo* or at the normal pressure. On the other hand, it was hardly possible to reach a

condition of constant weight by mere remaining over sulphuric acid at the ordinary temperature. Usually the loss of weight ceases after long standing over sulphuric acid *in vacuo*, but with some substances an exposure for several months is necessary.

2. Drying Liquids.—Liquids are dried by putting into them such substances as barium oxide, calcium bromide, chloride, iodide, or nitrate, quicklime, anhydrous cupric sulphate, potassium bisulphate, carbonate, or hydroxide, anhydrous potassium ferrocyanide, phosphorus pentoxide, silicon tetrachloride, sodium, sodium hydroxide (Ber. **25**, 145), fused sodium sulphate (Ann. **256**, 29), concentrated sulphuric acid, or zinc chloride (Ber. **24**, 1,019). If the liquid has a high boiling-point the water may be removed, according to Brühl, by passing carbon dioxide through it on the water bath.

Naturally such drying agents only will be used in any particular case as will have no chemical action on the liquid.

The commonest drying agent is *chloride of calcium*, which is fused before use to destroy its porosity. It forms compounds, however, with many substances. It cannot be employed, for example, for drying alcohol in the laboratory, as it forms an alcoholate which can only be decomposed by distillation from copper retorts. Propyl alcohol (Ber. **23**, 181) forms a compound of the formula $\text{CaCl}_2 + 3\text{C}_3\text{H}_7\text{O}$. Warm benzyl alcohol dissolves so much of it that the solution solidifies to a crystalline mass on cooling (Ber. **14**, 2,395), and Lieben (M. f. Ch. **1**, 919) states that the fatty acids likewise form crystalline compounds. Many esters like acetic ether and gluconic ether unite with calcium chloride. The compound with the latter has the formula $\text{C}_6\text{H}_{11}\text{O}_7 \cdot \text{C}_2\text{H}_5 + \text{CaCl}_2$.

An occasional disadvantage is that it does not always remove the last traces of moisture completely. Where this is important, as in determining exact boiling-points, sodium may be used for hydrocarbons and phosphorus pentoxide or sulphuric acid for other substances.

Calcium nitrate is used almost exclusively for drying unstable nitroderivatives and for nitrous anhydride,¹ while calcium iodide is employed for hydriodic acid gas (C. R. **112**, 717).

¹ If necessity arises for removing chlorine from a mixture of gases, they may be led over warm metallic antimony. Where carbon disulphide has to be eliminated the mixture should be led through a tube filled with rubber (Than, Ann. Suppl. **5**, 236).

On one occasion Ladenburg (Ber. **3** 305) used silicon tetrachloride to free acetic ether from the last traces of alcohol and water. Friedel and Crafts (Ann. Ch. Ph. [**4**], **9**, 5) state that heating ordinary alcohol at 100° with silicic ether converts it into absolute alcohol. Hartmann (Ber. **24**, 1,019) used zinc chloride for drying petroleum.

Wertheim (Ann. **127** 79) used glacial phosphoric acid for drying liquids.

It is often better to dry an ethereal solution than to attempt to dry the substance after distilling off the ether. Liebermann (Ber. **22**, 676), for example, dissolved hygrine in absolute ether, and added potassium hydroxide in order to get the base free from water and at the same time to avoid access of carbon dioxide from the air.

3. Drying Alcohol and Ether.—The chemist is often under the necessity of making *absolute alcohol* and absolute ether. In the former case the following are the special methods employed:—

(1) The alcohol is allowed to remain in a flask for two days (Z. Ch. **1865**, 260), with a large quantity of quicklime (Soubeiran, Ann. **30**, 356), and is then distilled off. The quicklime does not show much appearance of disintegration, but the alcohol, if the first and last portions which pass over are rejected,¹ is found to be absolute. It is not rendered red by potassium permanganate, but acquires only a faint brown tinge by contact with this salt.

(2) The flask containing ordinary alcohol and quicklime, which should be present in such quantity that some pieces project above the surface of the liquid, is connected with a reflux condenser and boiled on the water bath for an hour. The condenser is then reversed and the alcohol distilled off. In this case the lime falls to powder. The flask must not contain too much alcohol, as the heat developed by the formation of the hydrate may cause the alcohol to boil so violently as to be partly thrown out through the condenser.

If the alcohol contains more than five per cent. of water, this treatment must be repeated one or more times (Ann. **160**, 247). If it contains a large proportion of water, the alcohol is only half

¹ The rejection of the first fraction is necessary, because Soubeiran (Ann. **30**, 360) has shown that, even in the case of almost absolute alcohol, a product containing a larger proportion of water comes over first. On the other hand, Mendelejeff (Z. Ch. **1865**, 210) has shown that, on account of the rising temperature, the last portions are apt to contain moisture extracted from the hydroxide by means of the absolute alcohol.

filled with quicklime, as otherwise the flask may be broken by the violence of the hydration process.

Barium oxide (Jahresb. **1862**, 392) is exceedingly well adapted for the preparation of absolute alcohol. The removal of the last trace of water may be recognised by the liquid assuming a yellow colour. The oxide is made by the decomposition of the nitrate by a gradually increasing heat.

If a little barium oxide is added to the quicklime, as it is usually employed, the appearance of the yellow colour indicates the completion of the drying.

Vincent and Delachanel (C. R. **90**, 1,360) found that barium oxide could not be used for drying all alcohols since allyl alcohol gave a compound with it having the composition $2\text{C}_3\text{H}_6\text{O} \cdot \text{BaO}$. Hübner and Lellmann mixed such alcohols with three or four times their bulk of chloroform, and dried the solution with chloride of calcium.

Sodium and sodium amalgam are not adapted to removing water from alcohol because, according to Mendelejeff (Z. Ch. **1865**, 260), when they are used, traces of sodium and mercury are found in the distillate.

Raimundus Lullus attempted drying with potassium carbonate, but it is too weak to extract water from alcohols. Tornöe (Ber. **24**, 2,671) found that allyl alcohol still contained relatively large quantities of water after the ignited carbonate had removed all that it was capable of extracting.

(3) It will usually be found that, after the absolute alcohol has been distilled off, the glass flask containing a large mass of lime will be broken in the attempt to clean it. This disadvantage may be avoided by a process used by the author. Its working depends on the fact, ascertained by Squibbs (Z. analyt. Ch. **1887**, 94), that the laboratory method does not yield such pure alcohol as that employed in making it technically by filtration over quicklime in the cold. Such alcohol has a lower specific gravity than that obtained in any other way.

A cylindrical vessel between two and three times as tall as it is wide, holding twenty litres and provided with a stopcock at the bottom, is used. It is fitted internally with a perforated lining, having two handles at the top to facilitate its removal when necessary. In the centre, and attached to the inner cylinder, is a tube almost as tall as the vessel. The apparatus is filled with lumps of quicklime, and as much alcohol is added as it will hold. After remaining from ten to fourteen days the alcohol may be drawn off by the stopcock as absolute. The same lime may be used for three or four lots of alcohol, if fresh lumps are thrown in to make up for the subsidence. When the stopcock becomes

plugged by fine particles of the hydroxide, it may be cleaned out by a wire passed down the central tube. The apparatus can be suspended from the wall of the laboratory, and should always be kept filled with lime and alcohol.

The solubility of lime in alcohol is very small. Smith (Ar. Pharm. 1876, 356) found that 50 cc. of alcohol which had been in contact with lime for some time left, after filtration and evaporation, less than .005 grams of residue. So that alcohol made as above requires only filtration to render it sufficiently pure for most purposes. When distilled it contains over 99.9 per cent. of pure alcohol.



FIG. 19.

In this connection it may be remarked that, even when free from water, alcohol dried in these ways cannot be quite pure since alcoholic caustic potash prepared with it gradually becomes brown. According to Waller (Ch. Z. 1890, 23), the very purest alcohol does not possess this property. To get rid of these last traces of impurity, absolute alcohol is shaken with powdered potassium permanganate till it has acquired a distinct colour. It is then allowed to remain for some hours until the permanganate has decomposed and the brown oxide of manganese has separated out. Finally a little precipitated chalk is added, and the liquid is distilled with a Hempel tube in such a way that only 50 cc. pass over in twenty minutes. Ten cubic centimetres of the distillate are taken from time to time, boiled with a few drops of strong caustic potash, and set aside for twenty minutes. When a sample is obtained which shows no trace of yellow

colour by this test the distillation is continued and the alcohol preserved for use. The last portion must be rejected however.

Alcohol prepared in this way is perfectly neutral, and is suitable for making solutions of caustic alkalis or of silver nitrate. The solutions after boiling, or indefinitely prolonged standing, remain as colourless as distilled water.

Absolute ether is obtained from the commercial article by washing it with water, if necessary, to remove alcohol, then drying over chloride of calcium or phosphorus pentoxide, and finally boiling for some time with sodium in a flask attached to a reflux condenser. According to Squibbs (Ch. N. 51, 66 and 76), chloride of calcium

is alone capable of drying ether completely if they are left in contact for several weeks.

The presence of water may be detected by the cloud which is formed on mixing impure ether with carbon disulphide. Alcohol is proved to be present if the ether becomes coloured on shaking with aniline violet. Pure ether remains colourless.

CHAPTER VI

EXTRACTION

1. Extraction with Ether.—By extraction we mean the removal of a substance from a liquid in which it is dissolved or suspended, by dissolving it in another liquid which is not miscible with the first.

The liquids are usually shaken together in a separating funnel, and the resulting layers are then separated. Instead of such funnels, Schiff (Ann. **261**, 255) recommends the use of cylinders 400 mm. in length, and with diameters of 60 and 30 mm. They are provided with stopcocks and may be used for many other purposes in the laboratory, while their shape enables one to estimate the relative amounts of liquid and extracting medium being used.

Laboratory turbines are now in use for facilitating the agitation.

The liquids ordinarily used for extracting are: amyl alcohol, benzene, carbon disulphide, chloroform, ether, and petroleum ether; while acetic ether, phenol, and toluene are occasionally employed.

The number of times that the extraction must be repeated depends on the relative solubility of the substance in the liquid, usually largely water, in which it is contained, and in the extracting medium. Herb (Ann. **258**, 46), for example, found it necessary to extract an acidified solution of tetrahydroterephthalic acid no less than thirty times with ether. In general it is advisable to evaporate a portion of the last extract in order to see whether it has removed anything from the liquid. Where the extraction is difficult, it is sometimes possible to concentrate the liquid by evaporation before beginning the operation.

It should not be forgotten that 10 parts of water dissolve 1 part of ether, while 492 parts are necessary to dissolve 1 part of carbon disulphide. Those numbers apply, however, to pure water only,

and so, as the liquids to be extracted are most frequently solutions containing salts, the actual solubility will vary from case to case in practice.

When the liquid to be extracted is of a thick nature, or contains solid matter which might plug the stopcock of the separating funnel, the shaking is done in a strong bottle, and the liquids are not poured into the funnel till all suspended matter has settled. If an emulsion is formed on shaking, so that no clear separation into layers can be obtained, a small portion may be examined in a test tube to see whether the addition of more water or more ether will not bring about separation. Where this fails the addition of a small amount of alcohol is frequently useful. Indeed, ether containing alcohol (*Z. physiol.* Ch. **7**, 162) is often preferable to pure ether.

To assist the separation into layers, where acetic ether is used, Schröder (*Z. physiol.* Ch. **3**, 325) recommends the addition of common salt to the water solution, while others advise the use of calcium chloride.

On the other hand, ether may be used for separating some emulsions. Krämer and Spilker (*Ber.* **24**, 2,788) found that in washing synthesised lubricating oils emulsions were formed similar to those which are familiar in the case of natural oils of the same kind, and long standing had no effect in the way of separating them, although the addition of ether produced the desired result in a short time.

Liquids are known which cannot be extracted with ether directly at all. For example, the physiological chemist frequently desires to remove substances soluble in ether from the urine of animals which have been fed with drugs of various kinds. But it is seldom possible to extract the urine directly, as a more or less jelly-like mass is apt to be formed. In such a case, the urine is evaporated to dryness and the residue extracted with about one-and-a-half volumes of boiling alcohol for one volume of the original urine. On cooling, the alcoholic solution deposits much tarry matter, urea, etc. After 24 hours the liquid is poured off, evaporated, diluted with water, and either directly, or after the addition of alkali or acid, extracted with ether, acetic ether, or amyl alcohol.

Although this process is almost universally applicable, quite other methods for the examination of urines are sometimes preferred. Schmiedeberg and His (*Ann. Path. Pharm.* **22**, 255), for example, discovered one of the most extraordinary syntheses observed in the animal body—the conversion of pyridine, C_5H_5N , into methylpyridylammonium hydroxide, $C_5H_5N \begin{smallmatrix} \text{OH} \\ \diagup \\ \text{CH}_3 \end{smallmatrix}$ —

in the following manner. The urine was purified by the addition of lead acetate and ammonia followed by filtration, and the lead was removed from the filtrate with sulphuric acid. After this treatment a crystalline precipitate of a double salt of the base was obtained by adding a solution of potassium and mercuric iodides.

When solutions containing an acid, such as hydrochloric or acetic acid, have to be extracted, and the ethereal extract has an acid reaction in consequence of this, potassium hydroxide, or better still sodium, potassium, or calcium carbonate (Ber. **25**, 3,651) is added. If the extract contains organic acids in addition, the hydrochloric (Ber. **24**, 2,583) or acetic acid (Ber. **25**, 950) may be removed by shaking with water. Subsequent treatment with sodium carbonate solution gives the sodium salt of the organic acid free from sodium chloride or acetate. It is much better, however, to use tartaric acid or some other acid which will not be extracted by the ether for acidifying the solution in the first place.

Where the ethereal or other extract cannot be submitted to distillation for fear of decomposition, as happens in the case of alkaloids, a strong current of air is drawn through the liquid, or it is allowed to evaporate *in vacuo* over sulphuric acid and paraffin (A. Path. Pharm. **26**, 242).

Where the substance extracted by the ether is volatile in ether vapour, as is the case with Bamberger's dekahydroquinoline (Ber. **23**, 1,144), the vapour is caused to pass up through a Hempel's tube filled with glass beads (cf. Chap. IV., § 3) before entering the condenser.

Ether was found by Salkowski (Z. physiolog. Ch. **9**, 493) to take up traces of the sodium salts of volatile organic acids.

2. Extraction with Amyl Alcohol.—Amyl alcohol would be of wide application as an extracting agent if it could be easily obtained in a pure condition. The commercial article contains impurities which yield tarry matters under the influence of either acid or alkaline solutions, and the purification of the substances extracted is rendered more difficult on this account. Udransky (Z. physiolog. Ch. **13**, 248) has shown by an extended investigation that this unfortunate property is chiefly due to the presence of furfural which cannot be eliminated except by converting the alcohol into potassium amyl sulphate, and purifying this by repeated recrystallisation. The salt is decomposed by heating for five hours on the water bath with ten per cent. sulphuric acid, and the amyl alcohol is separated. Traces of acid are removed with calcium carbonate, and the product is distilled with steam.

Amyl alcohol is much used for the isolation of alkaloids, especially where small quantities, such as those found in cases of poisoning, have to be extracted and identified. Usler and Erdmann

(Ann. **120**, 121) were the first to show that vegetable bases are mostly very soluble in it, especially when it is warm. Since it boils at 132° hot water solutions may be extracted with it. They showed also that even large amounts of water containing a trace of alkali were unable to remove any of the alkaloids from solution in the alcohol. On the other hand, the hydrochlorides of the alkaloids were quite insoluble in the alcohol, and consequently shaking with water containing hydrochloric acid removed the bases completely.

When the substance cannot be recovered by shaking with water containing alkalis or acids, the alcohol is distilled off with the help of an oil or metal bath. This operation is best conducted *in vacuo* (Ber. **24**, 513).

Phenol was used by Bernthsen (Ann. **251**, 5) for extracting methylene red from the mother-liquor of methylene blue. By adding alcohol and ether to the phenol solution a mass of crystals was precipitated which could be purified by recrystallising from alcohol.

3. Solubility.—A substance shows often very different degrees of solubility in different extracting agents. For example, 1 part of hippuric acid dissolves in 200–270 parts of ether saturated with water at $20\text{--}25^{\circ}$, while it will dissolve in 16–22 parts of acetic ether under the same conditions. Bunge and Schmiedeberg (A. Path. Pharm. **6**, 237) found that this acid could be separated almost quantitatively from benzoic acid by shaking the solution of both acids in water with petroleum ether. The benzoic acid was completely removed while the other remained untouched. It has been shown that solanine (Z. analyt. Ch. **21**, 620) can be extracted from alkaline solution by amyl alcohol, while ether, benzene, chloroform, acetic ether, and petroleum ether have no such power.

4. Continuous Extraction.—This process is used in order to economise ether where the substance is not very soluble in it, or where a large amount of liquid is to be extracted. Neumann (Ber. **18**, 3,064), and still more recently Hagemann (Ber. **26**, 1,975), have suggested forms of apparatus for the purpose. We shall describe one of Neumann's (Fig. 20).

The ether is boiled in the flask B, and the vapour passes through the tube C into the liquid in the cylinder D. The extract accumulates on the surface of the liquid, while the condenser E serves to retain any uncondensed vapour. As soon as the ethereal layer has

risen above the highest point of the tube *f*, it is syphoned over into the flask B. The separating funnel *g* serves for the admission of the solution, while the stopcock *h* is used for its removal when exhausted.

It is well known that corks can be rendered perfectly vapour-tight only with great difficulty. When boiling ether or benzene are in question, Neumann (*Ber.* 18, 3,064) suggests the use of chromgelatine, as, after exposure to light, it becomes insoluble in the liquids ordinarily used. The parts of the apparatus which are to be made impervious by vapours, are simply coated with this substance by means of a small brush, and exposed to the light for two days. The chromgelatine is made by dissolving 4 parts of gelatine in 52 parts of boiling water, filtering, and adding 1 part of ammonium bichromate.

When small quantities of liquid have to be extracted, the much simpler Schwartz apparatus may be used.

The ether is boiled in the flask A, and its vapour passes through the tube B into an adapter of the form shown, and finally reaches the condenser D. The condensed ether flows from the adapter c

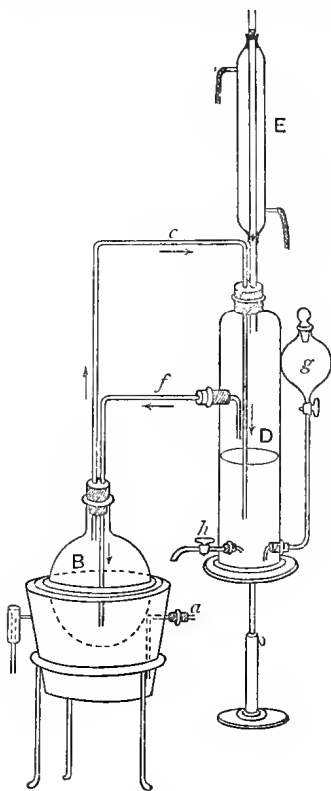


FIG. 20.

through the tube E to the bottom of the flask F, and, rising through the liquid to be extracted, accumulates on the surface until it flows over into the flask A by the bent side tube, thus completing the circuit.

5. Extraction of Solids.—For the extraction of solids, most of the liquids already mentioned may be used. Many forms of appa-

tus have been designed for the purpose. That of Farnsteiner (Fig. 22) is very useful, and its construction may be understood from the figure.

Its special advantage lies in the fact that the cooling arrangement is in the same tube with the substance under extraction, and

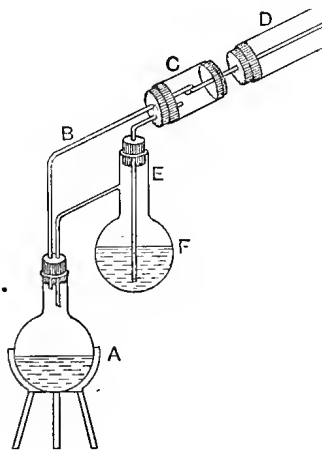


FIG. 21.

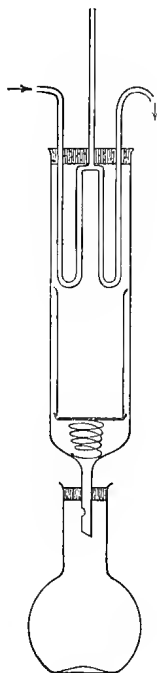


FIG. 22.

the number of joints is reduced to a minimum. The extraction tube is 32 cm. long, with a bore of 3 cm.

Reinsch's apparatus (Ch. Z. **1889**, 94) for extraction with cold ether is one of the best, and large quantities of material can be extracted at one operation. The ether traverses the tube B (Fig. 23) in the form of vapour, and after condensation runs into the vessel C, which fits loosely into the tube D, and after passing through the

mass to be extracted flows back into the flask A. A trap prevents the backward passage of vapour.

It may be mentioned here that ether sometimes explodes when distilled by itself, and that this has been ascribed to its containing an abnormally large amount of hydrogen peroxide or of ethyl peroxide (Proc. Chem. Soc. **1891**, 15). Such explosions are also known to occur during the evaporation of ethereal solutions, at about 60° , on the water bath. Schär (Ar. Pharm. **1887**, 623) has investigated the matter very fully. No test is known whereby it can be

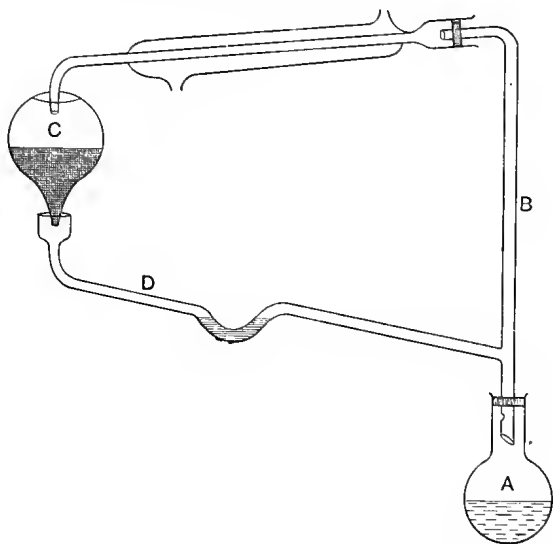


FIG. 23.

ascertained beforehand whether a specimen of ether is likely to explode or not.

6. Solvents and Diluents.—The use of proper media as *solvents*, for the purpose of bringing substances in contact with each other in such a way as to facilitate chemical action, may be discussed here since the liquids used are for the most part the same as those used in extracting and recrystallising.

The boiling-point of the solvent should be considered. If an

action takes place most easily at, say, 80° , it is advisable to use benzene in place of ether. Many expected actions fail to take place from improper choice of diluting media.

For example, Hofmann and Geiger, Martius, and Nietzky, were all unsuccessful in their attempts to prepare amidoazoparatoluene from paratoluidine in alcoholic solution. Nolting and Witt (Ber. **17**, 78) obtained the desired amidoazo-derivative with ease by carrying out the transformation of the diazoamidoparatoluene in paratoluidine solution.

Zetter (Ber. **11**, 169) states that phenanthrene gives different bromo-derivatives according as the action takes place in ether or in carbon disulphide solution. Pinner (Ann. **179**, 68) made bromine substitution products from aldehyde by using acetic ether as the solvent. He found that with carbon disulphide and carbon tetrachloride no definite derivatives could be isolated.

In making allyl cyanide from allyl iodide and potassium cyanide Rinne found (Ber. **6**, 389) that when ethyl alcohol was used for dilution a compound of allyl cyanide with the solvent was formed, having the formula $C_3H_5CN + C_2H_6O$, which boiled without decomposition at 173° – 174° . When he used allyl alcohol he got a substance having the composition represented by the formula $C_3H_5CN + 3C_3H_6O$.

In addition to the liquids used in extracting, many others are employed for diluting. *Glacial acetic acid*, for example, is used very commonly indeed. *Xylene* is less often employed. Bischoff (Ber. **24**, 1,046) added 120 cc. of xylene to 90 grams of methylmalonic ether, and then warmed the mixture with 11.5 grams of sodium, thus obtaining the sodium salt. Brühl (Ber. **24**, 3,378) had recourse to the same medium after he had found that the action of sodium on borneol was incomplete in ether or toluene solution. The same investigator (Ber. **25**, 1,873) diluted β -methylamidocrotonanilide with benzoic ether, when attempting to insert a benzoyl group by shaking with caustic soda and benzoyl chloride.

In endeavouring to condense chloral with derivatives of aniline, when chloral hydrate was applied, almost no result was obtained, but when chloral diluted with *phenol* was used the yield was almost quantitative. For example (Ger. Pat. 61,551), 14 parts of chloral were mixed with 9 parts of phenol, and 12 parts of dimethylaniline were allowed to flow into the mixture. After twenty-four hours a large amount of dimethyl-*p*-amidophenyloxytrichlorethane crystallised out (Ger. Pat. 49,844). Glycerol, dimethylaniline, and naphthylamine were used in the same way.

The dilution of liquids and solids with *Sand*, *Talc*, *Salt* (Ber. **25**, 3,031), &c., is no longer in favour.

In this connection, a discovery of Heusler's (Ann. **260**, 228) is worth mentioning. After having tried the use of sand during the decomposition of diazoamido-compounds to prevent explosion, he found that liquid paraffin was much more convenient. When diazoamidobenzene, or any of its homologues, is mixed with eight or ten times its weight of this substance, the diazo-body dissolves on warming, and a quiet evolution of nitrogen takes place as the heating continues.

It is frequently the case that solutions of *inorganic substances* are added to *alcoholic solutions* of organic bodies for the purpose of bringing about chemical action. As the use of solutions of the former in water generally gives poor results, it is advisable to select, where possible, salts which are soluble in alcohol. For bromide and iodide of potassium, the corresponding salts of sodium are preferably used, as they dissolve easily in alcohol. Tscherniac (Ber. **16**, 348) suggests the use of sulphocyanate of barium in place of the potassium compound. Cupric chloride, lead chloride, and lead acetate, are all soluble in alcohol. Gabriel (Ber. **24**, 1,112) purified ethylmercaptophthalimide by mixing its solution in hot alcohol with a similar solution of acetate of lead, to which a few drops of acetic acid had been added to remove the milkiness. The insoluble lead compound of the mercaptan was precipitated. No compound which fulfils the required condition is known which can take the place of potassium cyanide; possibly, the little known cyanide of calcium is such a substance. Cyanide of potassium is freely soluble, however, in 60 per cent. alcohol as well as in a mixture of 2 parts of alcohol and 1 part of concentrated hydrocyanic acid. But alcohol precipitates it from concentrated solutions in water. In all cases the so-called 100 per cent. potassium cyanide should be used, as the commercial article contains cyanate, whose presence gives rise to undesirable by-products.

CHAPTER VII

FILTRATION

FILTRATION is carried out in the same way as in inorganic chemistry. Ordinary filter paper is generally employed, but asbestos and other substances are frequently used.

The material for asbestos filters is prepared, according to Casamajor's receipt (*Ar. Pharm.* 1883, 377), as follows :—The asbestos is rubbed through a sieve with coarse meshes, and the material which has passed through is washed with a stream of water in a sieve with finer meshes to remove the smallest particles. It is then boiled with strong hydrochloric acid, thoroughly washed in a funnel containing a perforated platinum cone, and ignited in a porcelain crucible.

In organic work, however, many precipitates occur in such large quantities and of such a nature that they cannot be separated by decantation or with the help of the filter pump.

In such cases square pieces of cheese-cloth with a wide hem on all four sides are frequently used. Four strong pieces of string pass through the hems and hang free at the four corners. A frame is made of four pieces of wood somewhat longer than the sides of the cloth and united into a square in such a way that the ends project cross-fashion at the corners. The cloth is moistened before use to contract the meshes and prevent the precipitate running through, and bound by means of the strings to the frame so that it hangs down loosely in the middle. A vessel under the centre of the cloth, as it is distended by the weight of the precipitate, serves to catch the filtrate. The first portion to run through is usually milky, and is returned to the cloth. The filtration may be accelerated by stirring the precipitate.

The cloths will not last long if not carefully washed after use.

When the liquid cannot be made clear by filtration, lead acetate or subacetate, or if the liquid is neutral or alkaline, barium chloride and sodium carbonate (Z. physiolog. Ch. **9**, 493) may be added previously to assist in carrying down the precipitate.

Simple filtration has no effect in the case of putrefying liquids, as the bacteria pass through the pores of the paper and render the filtrate turbid. A clear filtrate may be obtained, according to a suggestion of Jolles (Z. analyt. Ch. **29**, 406), by shaking the liquid violently with tripoli.

By this means it is possible to clarify urine, which is cloudy from the presence of bacteria, and recognise the presence of traces of albumin in the filtrate by a very slight precipitate which appears on boiling, and does not redissolve on the addition of a drop of acetic acid. The tripoli takes up a small amount of albumin, however, just as charcoal retains a little grape sugar. It is hardly necessary to say that Chamberland's "bougies," Berkefeld filters, and similar devices employed in hygienic laboratories, yield filtrates free from bacteria, but they are not ordinarily used in chemical laboratories.

Filter-presses of size suitable for laboratory use are now obtainable. The method of working the press depends however on its construction.

In concluding this chapter it may be worth mentioning that, except where the use of distilled water is necessary, a very weak solution of a salt is often preferable for washing a precipitate, because where the former is used the solid is apt to be carried, to a small extent, through the filter. For example, Baeyer (Ann. **245**, 139) found that, in an oxidation by means of potassium permanganate in alkaline solution, the precipitated manganese dioxide was carried through the cloth filter by water in washing. On substituting water containing a little soda for distilled water this trouble was avoided. It is well known that clay will settle rapidly in river water while distilled water containing the same substance will remain cloudy for days. The principle is doubtless the same in both cases.

CHAPTER VIII

DETERMINATION OF MELTING-POINTS

1. Comparison of Methods.—We owe the first thorough investigation and comparison of the various methods of determining the melting-point to Landolt (*Z. physik. Ch.* **4**, 357). The methods he examined were :—

Melting and resolidification of large quantities, with the thermometer immersed in the substance.

Heating the substance in capillary tubes, and tubes of the form suggested by Piccard (*Ber.* **8**, 687), in liquid or air baths.

Löwe's method (*Z. analyt. Ch.* **11**, 211), by covering a platinum wire with the substance and warming it in a bath of mercury till the melting of the non-conducting film permits an electric current to pass. Christomanos (*Ber.* **23**, 1,093) has described a plan similar to this.

Landolt found that the first was the only thoroughly reliable method, and always led to constant results. About 20 gr. of the substance must be employed, however. When large quantities are used, the temperature of resolidification is easier to observe than that of melting.

To illustrate by means of a particular case, that of anthracene may be described. 18 grams of powdered anthracene were placed in a test tube of 30 mm. diameter and 175 mm. long, and this tube was surrounded by a larger one of about 40 mm. diameter. The whole was let down into a glass cylinder open at both ends, beneath which a lamp with annular flame was placed. The inner tube was closed with a cork through which the thermometer and a wire for stirring passed. The stirrer was operated by the hand as soon as melting began. Melting began at 196° and was complete at 197°. Resolidification began at 196.2°, but remained incomplete at a low temperature.

Melting-point determinations in capillary tubes of various forms show inaccuracy of different degrees for different substances. Sometimes the observed temperatures agree with the correct figures, but usually they are too high, especially when narrow tubes are used.

The results by the electrical method are also irregular and are frequently too high.

2. Heating in a Capillary Tube.—This method is the one usually employed in the laboratory, because very little of the substance is used for the determination in this way.

Reissert (Ber. **23** 2,241), who has studied the degree of accuracy attainable, states that the point when melting begins is the real melting-point, for the interior of the tube is always cooler than its walls, and the particles in contact with the latter melt nearest to the correct temperature. It is therefore often advisable, after charging the tube, to shake out the contents and notice when the particles which remain adhering to the sides melt.

A thin-walled capillary is chosen, charged with some of the substance and attached to the thermometer by means of a rubber ring or platinum wire, so that the substance is close to the bulb.

The thermometer is suspended in a test tube, which is then filled for 2 cm. of its height with concentrated sulphuric acid, or may be left empty to serve as an air bath. The test tube is itself immersed in a flask containing sulphuric acid. The flask is gradually warmed, and as soon as the substance in the tube melts the temperature is read.

The double bath, which was first suggested for this purpose by Gräbe (Ann. **238**, 320), insures uniform heating of the acid or air contained in the inner tube. When the thermometer is placed directly in sulphuric acid in a flask or beaker, even if the acid is stirred or shaken, the heating is not uniform and the result is inaccurate.

If glycerol is used in place of sulphuric acid there is less chance that the rubber ring will colour the fluid brown even at high temperatures. It is better, however, to fasten the capillary by means of a suitably bent loop of platinum wire.

Many chemists use glycerol in all cases instead of sulphuric acid. For substances which melt below 100° C. water is frequently employed. In the particular case of fats a capillary, open at both ends, is dipped into the melted specimen, and, after solidification is

complete, is attached to a thermometer in the usual way. Both are then placed in a vessel of water, and the temperature at which the melted fat and the water rise in the capillary is taken.

3. Influence of Impurities.—It is found that impurities almost always depress the melting-point a relatively large amount. The opposite hardly ever occurs, although Wallach (*Ber.* **25**, 919) mentions that impure specimens of camphor derivatives melt higher than the same substances in the pure state.

4. Peculiarities in some Classes of Bodies.—Some classes of bodies show peculiarities in the matter of melting-point. Isomers, for example, which have almost identical melting-points, become widely separated in this respect when converted into acetyl derivatives. Hydrazones (*Ber.* **23**, 1,583) must be rapidly heated to get constant observations.

The addition product of hydrochloric acid and turpentine, $C_{10}H_{16}HCl$, loses the acid so easily that to find its melting-point (Riban, *Bull. Ch.* **24**, 14) it had to be sealed up in a capillary filled with hydrochloric acid gas. Chloranil sublimes completely below the melting temperature, but Gräbe (*Ann.* **263**, 19), by sealing it up completely in a capillary tube, ascertained that it melted at 290° .

CHAPTER IX

DETERMINATION OF MOLECULAR WEIGHTS

THREE methods are at present in use for determining the molecular weights of organic bodies.

1. By measuring the vapour density.
2. By Raoult's method of measuring the lowering of the freezing-point of a solution.
3. By Beckmann's method of measuring the elevation of the boiling-point of a solution.

1. By Measuring the Vapour Density.—The application of measurement of the vapour density depends on the following considerations. According to Boyle's and Charles's laws, all gases behave equally in their relations to temperature and pressure. This is explicable only on the hypothesis that equal volumes of all gases contain equal numbers of molecules. Consequently the molecular weight is found by comparing the specific weight of the gas with that of hydrogen, which is selected as having the smallest specific weight. Since, however, to the specific weight of hydrogen is assigned the value one, while its molecular weight is two, the molecule of hydrogen consisting of two atoms, the molecular weights of other gases are obtained by multiplying their specific weights by two.

The molecular weights of such substances as are permanent gases at ordinary temperatures can be determined by direct weighing of a known volume. As, however, we have no balances capable of weighing directly the vapours of substances which require an elevation of temperature to bring them into this form, various methods of determining the vapour density have been devised

where measurements are made, from which the desired information can be obtained by calculation.

The plans suggested for carrying out the determination have been numerous. Those recommended by Victor Meyer (Ber. **15**, 2,777, to whom we owe the most convenient methods, and whose opinion will be regarded by all as decisive on this subject, are here described.

(1) Where the substance boils not higher than 260° , and can bear heating about 30° over its boiling-point, the method by expulsion of mercury devised by Victor Meyer is in every way suitable, whether we consider the accuracy of the results, the small amount of mercury required (about 35 cc.), or the simplicity of the operation. Of course the substance must be without action on mercury. For heating, water, xylene, aniline, ethyl and amyl benzoates and diphenylamine are used.

(2) Substances which cannot be vaporised without decomposition under atmospheric pressure, or which will not bear heating above their boiling-points, may be examined by Hofmann's method, provided they boil below 310° and do not attack mercury.

(3) For difficultly volatile substances, which boil between 260° and 420° , and do not act on metals, Victor Meyer's method, depending on the expulsion of Wood's alloy, may be employed.

(4) To determine the vapour density where the substance boils at a higher temperature than this, or where it attacks mercury, Victor Meyer's air expulsion method must be used.

(5) Demuth and Victor Meyer (Ber. **23**, 311) have described yet another method which may be used where substances can only be volatilised under diminished pressure. Other suggestions applicable to such cases have been made by Eykman (Ber. **22**, 2,754), and by Schall (Ber. **25**, 1,491).

(1) Description of method where the quantity of *mercury expelled by the vaporised substance is measured* (Ber. **10**, 2,068'. The liquid whose vapour is to heat the substance, and of which only 50-60 cc. are necessary, is contained in a thin-walled glass vessel, whose bulb has about 80 cc. capacity, and whose neck is 750 mm. long by 42 mm. diameter. The frequent heating and cooling of the bulb are apt to make it brittle, and it has a tendency to break after repeated use. To avoid this Victor Meyer (Ber. **19**, 1,862) suggests the use of a cast-iron crucible whose margin is so made that a glass cylinder rests in a groove, which is filled with mercury to render the joint air-tight. Such a mantle will hardly ever break, and, if it does, can easily be replaced.

The construction of the thin glass vessel A, which contains the substance under examination, may be understood from the figure (Fig. 24). It holds about 35 cc., and the narrow limb has a diameter of 6 mm. It is kept in a vertical position by a wire, and

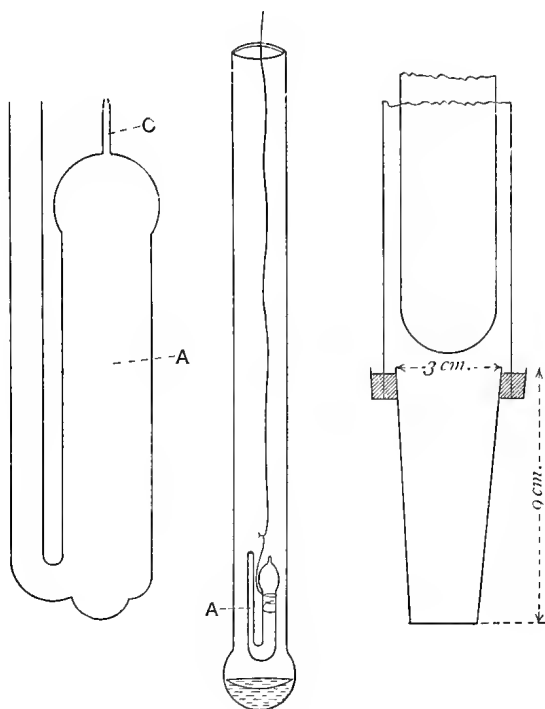


FIG. 24

hangs from a hook on a long and somewhat stouter wire, which is supported by a stand. When the determination is carried out, a known quantity of the substance is placed in the vessel and the whole weighed correctly to $\frac{1}{10}$ gram. In order to introduce the substance conveniently, it is weighed out, if a liquid, in a small

Hofmann tube. Following a suggestion of Brühl's (Ber. **9**, 1,371), Victor Meyer employed always the same size of tube and partially filled it with mercury when a smaller quantity of the substance was to be used. When the substance is solid, a small open tube answers the purpose better. The glass vessel A is next completely filled up with mercury, and, after the capillary has been sealed, is weighed once more and lowered into the outer tube by the wire.

The liquid is now heated to boiling. When the jacket contains water, some of it will escape uncondensed, but in the case of aniline and other substances of high boiling-point the vapour will only rise a short distance above the vessel containing the substance. After mercury is no longer expelled, the vessel is drawn out again, and, when cold, is weighed. The height of the barometer and the original temperature of the mercury, which will be that of the air, being known, it remains to measure the pressure which the mercury column in the narrow limb of the vessel exercised. The capillary is opened, and by inclining the vessel the mercury is brought up to the top of the narrow limb, and a mark is made showing the level of the mercury in the wide limb. The difference in height between this point and the top of the narrow limb at the temperature of the air is measured, and is added to the reading of the barometer to find the total pressure. It is necessary finally to determine the volume of the Hofmann tube by measuring the weight of mercury which it will hold. The vessel A may be used repeatedly if the capillary is preserved.

The result is calculated by means of the formula :

$$d = \frac{S(1 + 0.00366T) \times 7988000}{(P + p - s)[(a + q)\{1 + 0.0000303(T - t)\} - r\{1 + 0.00018(T - t)\}](1 + 0.00018t)}$$

where S = Weight of substance taken,

T = Temperature of vapour-mantle,

t = Temperature of the air,

P = Barometric pressure reduced to 0° C.,

p = Height of mercury column in the vessel,

s = Tension of mercury vapour at temperature T,

a = Weight of mercury first taken,

q = Weight of mercury which the little tube will hold,

r = Weight of mercury remaining in the vessel after the heating.

0.0000303 is the coefficient of expansion of glass, and 0.00018 that

of mercury. (For temperatures above 240° C. the value 0.00019 must be used.)

The temperature of the vapour-mantle does not require to be determined, as the boiling-points of the liquids used are known. Meyer states that for amyl benzoate the temperature is 253° C., and for diphenylamine 290° C. The difference between these values and the values of the boiling-points usually given is due to the fact that here these substances are mixed with mercury while boiling.

(2) *Description of Hofmann's Method* (Ber. **1**, 198, and **9**, 1,304). A tube about 1 metre in length is sealed at one end, filled with mercury, and inverted in a trough. The mercury descends in the tube, leaving a vacuum about 25 cm. long, and the height of the mercury column above the level of the free surface is measured, giving the barometric reading. It is essential that the tube and the mercury should be perfectly clean¹ and dry. One of Hofmann's small stoppered glass vessels is next filled with a known quantity of the substance, and is put into the tube, which is then enclosed in the mantle. The vapour of the boiling liquid enters at the bottom (Fig. 25), and whatever part condenses flows back into the flask. A part will also escape as vapour at the top. As the substance becomes volatilised the level of the mercury is depressed. When the column has become stationary, a cathetometer is set at the level corresponding to the height of the column, and when the mantle and tube are cold the former is removed and a strip of paper is pasted on the tube at the level indicated by the cathetometer. In this way the volume which the vapour occupied during the experiment is registered. To ascertain what this volume was, the tube is afterwards filled with mercury up to the mark, and this quantity weighed to within 0.5 grams. The volume in cubic centimetres is obtained by dividing this by the specific gravity of mercury.

In addition to the barometric height at the beginning of the experiment, it is necessary to measure the height of the mercury when the column had descended to the point at which it became stationary.

The measured volume which the vapour occupied is reduced to 0° and 760 mm. pressure. This correction is included in the following formula. The density is given in terms of hydrogen as unity.

¹ Mercury is best purified by distillation *in vacuo* in the glass apparatus devised by Weinhold, which requires little attention and yields about 1 kilogram per hour.

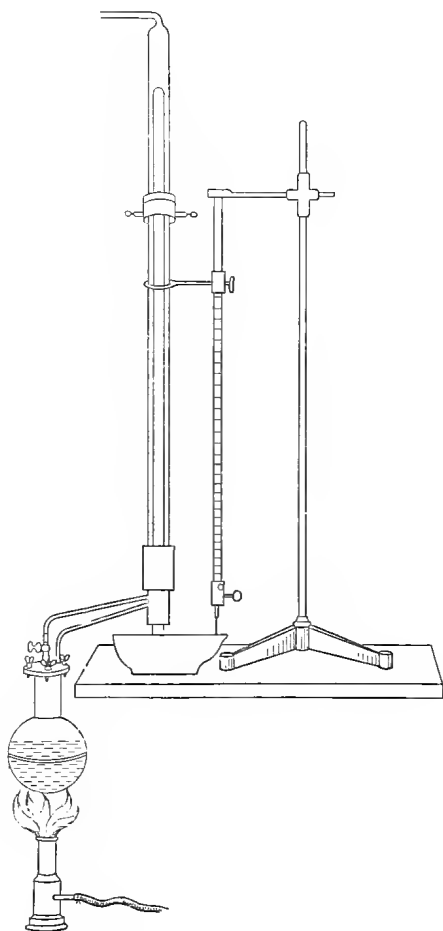


FIG. 25.

$$D = \frac{760(1 + 0.00365t')p}{V \times 0.0012934 \times B}$$

$$B = \frac{b}{1 + 0.00018t} - \left(\frac{b'}{1 + 0.00018t'} \times \frac{b''}{1 + 0.00018t''} + s \right)$$

where D = value of the density sought,

V = volume of the vapour at t' ,

t = temperature of the air,

t' = temperature of the vapour-mantle,

t'' = temperature of the mercury column not heated by the vapour,

p = weight of substance taken,

b = height of the barometer reduced to 0° ,

b' = height of the column below the vapour-mantle,

b'' = height of the column within the heated vapour at the temperature t' ,

s = vapour tension of mercury vapour at t' .

Vapour Tension of Mercury Vapour in Millimetres (Regnault).

Temp.	Tension.	Temp.	Tension.	Temp.	Tension.
100°	. . 0.75	180°	. . 11.00	260°	. . . 96.73
120°	. . 1.53	200°	. . 19.90	280°	. . . 155.17
140°	. . 3.06	220°	. . 34.70	300°	. . . 242.15
160°	. . 5.00	240°	. . 58.82	320°	. . . 368.73

(3) Description of method where the quantity of *Wood's alloy expelled by the vaporised substance* is measured: for use in the case of substances which are volatilised without decomposition at 444.2° (boiling-point of sulphur), and do not act on Wood's alloy (Ber. 9, 1,220).

The substance is weighed out in a small vessel like that in Fig. 26, which shows the natural size. The vessel is selected according to the expected molecular weight, where this is small a smaller vessel being taken, so that the volume of vapour produced may always be smaller than the volume of the bulb. The vessel is slightly bent to enable it to pass easily into the bulb.

To fill the small vessel, which has been previously weighed, it is bound to a platinum wire, and is pressed beneath the surface of a quantity of the melted substance contained in a narrow test tube. Any air bubbles which may remain in it are removed by shaking, or warming, or by touching them with a fine capillary tube. The vessel is then drawn out, and when the substance has solidified is

released from the wire, wiped with a silk cloth, and weighed again. If there is too little of the substance for this method of filling, it may be melted in the vessel itself. A stoppered tube is used for liquids. For solids no stopper is required, as they adhere firmly to the vessel and there is no danger of any being lost. The bulb apparatus is very carefully cleaned before the substance is introduced.

After the small vessel containing the substance has been introduced, the apparatus is weighed correctly to 0.1 gram. It is then

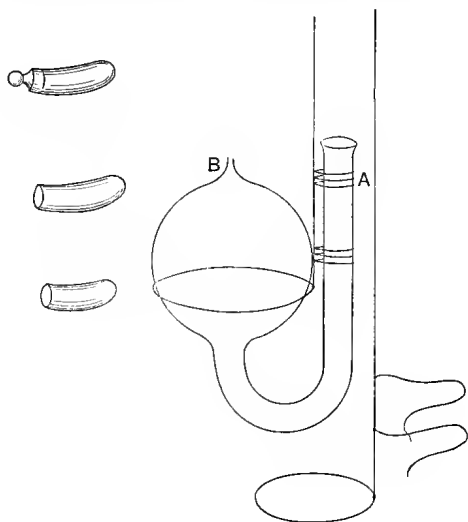


FIG. 26.

held by a clamp attached to the limb A, while the Wood's alloy is poured in. The alloy is brought to a temperature of about 100° before being used. During the filling the apparatus must be so inclined that the vessel containing the substance passes up into the bulb and not into the other limb.

The alloy, if it has not previously been used, must be boiled several times, first with benzene and then with alcohol, and is finally heated on the water bath with constant stirring till dry. If it has been used for similar determinations before, it is simply extracted

with alcohol and dried. It is best kept in a porcelain evaporating dish, in which it is allowed to solidify, and preserved in a desiccator to exclude moisture. When required for use it is melted on the water bath, and heated by a small flame to 150° – 180° , to expel every trace of moisture, and after it has cooled once more to about 100° is ready for use. Meyer suggests the wearing of a leathern glove when handling the dish containing the melted alloy.

After the apparatus is filled with the alloy some bubbles of air may remain attached to the sides. By judicious shaking and tapping they are brought to the top and escape through the capillary B. Small traces of air remaining do not appreciably influence the determination. When the apparatus is finally filled the capillary is sealed. In order that the apparatus may be just filled with alloy at 100° , it is now suspended in a beaker of boiling water by a wire similar to that described later, but lacking the thinner wires for binding it securely. A few drops of the metal will be expelled. After a few minutes the apparatus is removed from the beaker, and any water or protruding globule of metal is removed from the open limb by means of a piece of filter paper. It is dried carefully, weighed again correctly to 0.1 gram, and bound by means of thin piano wire to a stout iron wire in the way shown in the figures. All of these operations are as easy to carry out as if the apparatus were filled with mercury. Before the second weighing the metal solidifies. It must not be allowed to cool completely, as it cracks the apparatus. This does not happen, however, till it has stood for about forty-five minutes.

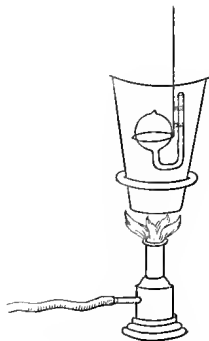


FIG. 27.

The heating in sulphur vapour takes place in a cast-iron crucible holding about 400 cc., and containing 120–130 grams of sulphur. The apparatus is hung in the middle of the crucible, which is covered by a perforated lid, and heated by means of a quadruple Bunsen burner. When the sulphur boils the vapour issues beneath the lid, and burns in a large flame half a foot high. The experiment must therefore be carried out in a hood provided with good ventilation.

After about twenty-five minutes the flame is extinguished, the lid removed, and the apparatus drawn out. The level of the metal in

the bulb is marked immediately by touching the glass with a little sealing-wax adhering to the end of a glass rod. A permanent mark remains which enables the observer, after the cooling and weighing are accomplished, to measure the height of the column of alloy to whose pressure the vapour of the substance was subjected. As the specific gravity of the alloy at $444^{\circ}2'$ is to that of mercury in the ratio 2 . 3, the number of millimetres found is multiplied by two thirds, and the result added to the barometric pressure. Before weighing, the apparatus is carefully wiped with filter paper.

The density of the vapour is obtained from the formula :—

$$D = \frac{S \times 14146000}{(a - 0.036b)(P \times \frac{2}{3}p)}$$

D is the density, that of air being unity ; S is the weight of the substance taken ; b is the weight of alloy taken, and a that of the quantity expelled ; P is the barometric pressure, and p the height of the column of alloy ; 0.036 represents the proportion of the alloy lost through expansion.

As the metal is not attacked by sulphur, the portion extruded is recovered by pouring off the sulphur before it solidifies, and the bulb is broken to recover the alloy contained in it. The weighing tube is cleaned with boiling nitric acid.

The Wood's alloy which Meyer used (Ber. **9**, 1,217) consisted of bismuth (15 parts), lead (8 parts), tin (4 parts), and cadmium (3 parts). It melts below 70° , and can be as easily manipulated as mercury ; it is not attacked by most organic bodies in a state of vapour, and it can be very easily purified from substances which become mixed with it in course of use.

(4) Description of method where the *air expelled by the vaporised substance* is measured (Victor Meyer).

The apparatus (Fig. 28) consists of an inner tube like that in the figure, of about 100 cc. capacity, closed at the top by a rubber stopper, which is always pushed in to the same extent. This stopper has been replaced by a stop-cock in later forms of the apparatus. An outer tube contains the heated vapour-mantle, and when a high temperature is required a metal bath can be substituted. A side tube a permits the escape of air driven forth by expansion. When the temperature has become constant and no more air bubbles appear, a graduated glass tube filled with water is inverted over the end of the side tube, and the tube being opened at d , the portion of the substance weighed out is dropped in, and

the tube rapidly closed. The temperature being high enough, the substance is volatilised, and a quantity of air corresponding to the volume of the vapour is expelled into the graduated tube, where it

can be measured. In order that the little vessel containing the substance may not break the tube, the bottom of the latter is covered with sand or asbestos. When the vaporisation is rapid and the quantity of the substance is so small that only the lower part of the apparatus is filled with its vapour, the error owing to diffusion of the vapour will be negligible.

The following points about the apparatus deserve description. The side tube *a* is made as small as possible. It is 1 mm. in diameter and 140 mm. long. The quantity of substance taken must be such that its vapour will fill less than a half of the bulb *b*. This bulb is 200 mm. long, and holds about 100 cc. It is attached to a tube 600 mm. long, and 4-6 mm. internal diameter. The side tube *a* is connected with the tube at a height of 500 mm. For temperatures up to the boiling-point of diphenylamine (310°), a glass outer vessel is used with a bulb of 80 cc. capacity and a neck 520 mm. long and 40 mm. in diameter. The mantle is therefore the same as that used for the first method. The vapours employed

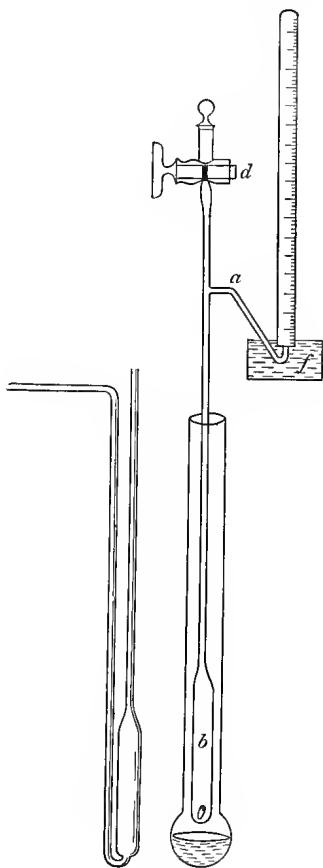


FIG. 28.

are water, xylene, aniline, ethyl benzoate, amyl benzoate, and diphenylamine. Ladenburg (Ber. **21**, 762) used anisol on one occasion. These bodies do not require to be pure, as mixtures boiling under

such conditions yield constant temperatures, and the exact temperature used does not enter into the calculation.

For temperatures above 310° , iron tubes (Ber. **17**, 1,335) made from pieces of gas pipe welded up at the end, and containing anthracene (b.-p. 335°), anthraquinone (b.-p. 368°), and sulphur (b.-p. 444°), are kept in readiness. For still higher temperatures (518°), an iron tube charged with phosphorus pentasulphide¹ is employed. As this substance will not stand long exposure to the air, it is prepared freshly each time it is needed by melting together two parts of red phosphorus with five parts of sulphur. For still higher temperatures a bath of molten lead can be used (Ber. **11**, 2,255), but this is seldom necessary in organic work.

In making a determination, the inner tube, whose volume does not require to be known, is introduced into the mantle. As was mentioned above, the bottom of the inner bulb should be covered with a layer of asbestos, sand, or mercury, to break the fall of the vessel containing the substance. The end of the side tube opens beneath the surface of the water in a small trough. As soon as the temperature has become constant, the substance is dropped in and the graduated tube is placed over the end of the side tube at the same instant to catch the expelled air.

If the apparatus is provided with the arrangement suggested by Mahlmann (Z. physik. Ch. **1**, 157), which is shown in Fig. 28, the vessel containing the substance is allowed to drop into the tube from the small chamber at the top by simply turning a stop-cock provided with a large passage way. Even if the tube has to be closed by an ordinary rubber stopper, however, the withdrawal of the latter to introduce the substance may be avoided by using the arrangement in Fig. 29 (Noyes). A glass tube closed at one end passes through the stopper, and in it is placed the tube containing the weighed portion of the substance. The latter is supported by a bent wire in such a way that it can be released at the proper moment and allowed to drop into the bulb.

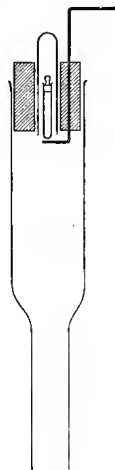


FIG. 29.

After about fifteen seconds the substance begins to volatilise, and when no more bubbles issue from the tube the stopper is removed,

¹ The first application of phosphorus pentasulphide for this purpose was made by Hittorf (Pogg. Ann. **126**, 193).

and the graduated cylinder is placed in a deeper vessel, so that the water reaches the same level without and within. After a little time the volume is read off and the temperature of the water and height of the barometer are noted.

$$D = S \frac{(1 + 0.003665t) \times 587780}{(B - w)V}$$

where S = the weight of substance used,

B = the height of the barometer reduced to 0° ,

w = the vapour tension of water vapour at the temperature t ,

V = the measured volume of air,

t = temperature of the water or of the air.

In many cases solids can be used in the form of little cylinders instead of being enclosed in small vessels of glass. When the substance is fusible, such cylinders are very easily made (Ber. **23**, 313). The substance is melted in a dish and drawn up into a short tube about 2 mm. in diameter. When it is cold and once more solid, it will adhere only partially to the tube. After gentle heating in a small flame it may be pushed out of the tube by a wire without its shape being destroyed. Victor Meyer recommends the employment of substances in this form very strongly, as the weighing out and introduction into the apparatus are greatly simplified by their use. More than 0.1 gram should not be employed so that the vapour may always occupy less than 50 cc.

When the substance is acted on by oxygen, the apparatus is filled with dry nitrogen before the experiment by leading a stream of the gas through a tube which passes to the bottom of the apparatus. Better still, a form of the apparatus shown in the figure may be used where a tube for the admission of the nitrogen is fused into the bottom of the bulb (Ber. **21**, 688).

Meyer made the nitrogen by Gibbs and Böttger's process¹ by boiling a solution of one part potassium bichromate, one part ammonium nitrate, and one part commercial sodium nitrite in three parts of water. He found it advisable to pass the gas over red-hot copper to remove all traces of oxygen.

(5) Description of method for determination of the vapour density of a substance at a *temperature below its boiling-point* (Demuth and Meyer, Ber. **23**, 311).

The method of Hofmann already described attains the same end as the present method, and, on account of the accurate results which it yields, will always be a favourite when the properties of the substance permit its use.

¹ Jahresb. d. phys. Vereins zu Frankfurt a. M. **1876-77**, 24.

Since Victor Meyer's method by expulsion of air was invented, chemists have striven to increase the simplicity and convenience of the operation, yet the methods introduced never quite equalled Hofmann's in these respects. The first hints of this fifth method are to be found in the report of the sixty-second meeting of the "Gesellschaft deutscher Naturforscher" (corresponding to the "British Association"), at Heidelberg, in 1889. The idea rests on the fact that in the ordinary determinations by air expulsion, a certain amount of mixing of the vapour with the air above it always takes place, and therefore a reduction of the pressure of the vapour considered by itself. If the vapour diffuses sufficiently rapidly, this reduction may be equivalent in effect to the action of an air pump, or to the mercury column in the Hofmann method. When the vessel is filled with air, indeed, this effect does not come into play appreciably, but with an atmosphere of hydrogen, the more rapid diffusing power of this gas leads to a remarkable lowering of the temperature necessary for volatilising the substance.

When used for this method the bulb has a capacity of about 100 cc. and a diameter of 3 cm. The bottom is rather strong and somewhat flat in form so as to facilitate the spreading out of the substance and its evaporation. The stem is not more than 4-5 mm. wide. The amount of the substance must be taken so that the amount of expelled gas may be between 9 cc. and 11 cc.

The introduction of the substance in suitable form may present some difficulties. If it can be cast in small cylinders it will melt and spread itself on the floor of the bulb without further trouble. In the case of liquids some kind of vessel is essential. A small, very thin tube made of Wood's alloy, as it melts on reaching the hot bulb, is very serviceable. The necessary lightness may be attained by filing the outside of the vessel down. In any case it should be dropped repeatedly into the tube before the experiment so as to be sure that the bulb is strong enough to withstand the impact. If it chance that the substance whose examination is in hand acts chemically on the alloy, or if the temperature is below its melting-point, then recourse must be had to a wide, loosely stoppered glass tube.

It must be mentioned that asbestos or sand cannot be used for protecting the bottom of the bulb, as they soak up the melted substance and prevent its volatilisation. Demuth and Meyer used small spirals of platinum wire in a few cases, but with sufficiently thin vessels protection is seldom necessary. Where it is admissible a thin layer of mercury is sometimes useful.

When this method is used, the same values for the vapour density are obtained, at temperatures considerably below the boiling-point of the substance, as were formerly obtained by heating several degrees above it. For example, xylene gave the value 3.73 40° below its boiling-point, and naphthalene 4.65 35° below its boiling-point, where the calculated values were 3.68 and 4.44 respectively. These values are calculated for air and not hydrogen as unity.

In calculating, the same formula as before is employed.

Schall (Ber. **25**, 1,491) and Eykman (Ber. **22**, 2,754) have likewise suggested methods for determining the vapour density under diminished pressure, which can be used instead of Hofmann's or Demuth and Meyer's.

2. Raoult's Method.—The *measurement of the lowering of the freezing-point of a solvent* has only come into use during the past few years as a means of determining the molecular weight. But the fact that the vapour density method can only be applied when the substance can be volatilised without decomposition, while the new method is applicable to almost all substances of which suitable solutions can be prepared, has led to its rapid introduction in every laboratory.

It was found by De Coppet and Raoult (Ann. Ch. Ph. [**5**], **28**, 133; [**6**], **2**, 115), that when a known amount of a substance was dissolved in a measured quantity of a solvent (such as benzene or glacial acetic acid), the lowering of the freezing-point of the latter produced by the presence of the former was a function of the molecular weight of the dissolved substance.

Various forms of apparatus have been devised for carrying out the determination. The principal ones were those of Auwers (Ber. **21**, 701), Hollemann (Ber. **21**, 860), Hentschel (Z. physik. Ch. **2**, 306), Beckmann (Z. physik. Ch. **2**, 638), Eykman (Z. physik. Ch. **2**, 964; **3**, 113 and 203; **4**, 497), and von Klobukow (Z. physik. Ch. **4**, 10).

Beckmann's apparatus is widely used and is very convenient. Its construction is shown in Fig. 30.

The tube A holds the solution to be frozen, and has a capacity of about 25 cc. up to the side tube. A delicate thermometer graduated to hundredths of a degree passes through the rubber stopper of this tube, as does also a stout platinum wire for stirring. This tube is placed in a somewhat wider tube B so as to be surrounded by an air jacket. The whole is suspended in a wide battery jar C, which

contains cold water or a freezing mixture, the temperature of which is selected so as to be from 2° to 5° below the freezing-point of the solvent. A cover and stirrer are provided for this outer jar.

The inner tube, containing a few clippings of platinum foil, is weighed charged with about 15 grams of the solvent, and weighed again. The apparatus is then put together, and the freezing-point determined.

In practice the temperature has always to be carried below the actual freezing temperature, before the formation of crystals begins. The platinum is added, and constant stirring is kept up in order that this over-cooling may be as small as possible. The crystals should always appear in the liquid. If the over-cooling has been excessive, a thick crust may be formed on the side of the tube and, on account of the concentration of the rest of the solution, too low a temperature will be read off. When crystallisation begins the temperature rises to the real freezing-point, and when the mercury column has come to rest the reading is made. The frozen material should then be remelted, and the operation repeated as a check on the first result. This precaution should be observed all through the determination.

The thermometer demands special description. If it were of the common construction, it would require to be extremely long and unhandy so as to be applicable with different solvents, such as water, benzene, and acetic acid, and still be divided into hundredths

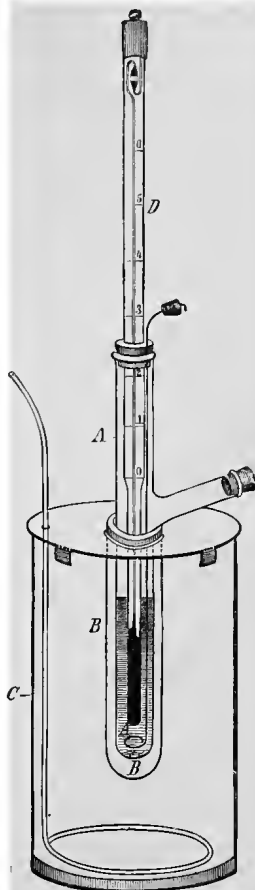


FIG. 30.

of a degree. The only alternative would be to employ a different thermometer for each solvent. For the present use, however, it does not require to show actual temperatures but only differences of temperature. The scale is therefore constructed to show only six degrees. The capillary is provided with a small reservoir for mercury at the top, and the instrument is filled in such a way that at 0° the mercury almost reaches the top of the scale. If it is to be used in the neighbourhood of a higher temperature—say 16° —the instrument is warmed to 18° or so, and the mercury which has flowed into the reservoir is separated from the column by cautious tapping with the finger. Slight cooling will now bring the end of the column back on to the scale, and temperatures between 11° and 17° may be read off. A similar adjustment can be made for any desired temperature.

A known quantity of the substance, which is contained in a weighing tube, or in the case of a liquid, in a pycnometer, is introduced through the side tube; the amount to be taken is regulated by the depression which it will produce. A depression of less than 0.2° is of no service, as the experimental errors will render the result unreliable. With a depression of from 1° to 2° the error will not be more than one or two per cent. It is desirable also to make several observations at different concentrations; a suitable series may be obtained by adding the substance in three or four portions, weighing the tube and determining the freezing-point after each addition, in such a way that depressions ranging from 0.2° to 2° are obtained. Dissociation will sometimes be brought to light in this way.

The molecular weight is calculated from the formula :—

$$M = c \frac{\phi}{t}$$

where M is the molecular weight, c the constant for the liquid, ϕ the percentage of the substance contained in the solvent, and t the depression of the freezing-point in degrees Centigrade.

The following table gives the values of the constant for the solvents most commonly used :—

Benzene	49	Diphenylamine . .	88
Glacial acetic acid .	39	Naphthalene . . .	69
Nitrobenzene . . .	71	Naphthylamine . .	78
Phenol	74	Palmitic acid . . .	44
Water	18.9	<i>p</i> -Toluidine	51
Formic acid	27.7	Thymol	92

A solvent must be chosen which will have no chemical action on the substance under examination.

The values obtained are never quite accurate, because the molecular depressions are not quite constant for any solvent ; but taken with the results of analysis they always make it abundantly clear what formula must be selected. For example, Baumann and Fromm (Ber. **24**, 3,595) proved by its help that the polymer of thiofurfurol possessed a molecular weight eighteen or twenty times as great as the empirical formula indicated.

Eykman's apparatus (Z. physik. Ch. **2**, 964) is much simpler than Beckmann's, but it gives less accurate results ; it has the advantage, however, of working equally easily with solvents of high melting-points, such as phenol, thymol, naphthalene, and diphenylamine ; with Beckmann's apparatus a beaker of warm water must be substituted for the jar in such cases.

Fabinyi (Z. physik. Ch. **3**, 38) uses the depression in the melting-point of a well-known substance, such as naphthalene, which is produced by the addition of a known proportion of the substance under investigation, for calculating the molecular weight of the latter. A minute amount of the substance suffices for the determination.

3. Beckmann's Method by Measuring the Elevation of the Boiling-Point of a Solvent.—Using an idea suggested by Raoult's work, Beckmann has worked out a method by which the elevation in the boiling-point of a liquid, produced by dissolving any substance in it, can be used for the determination of the molecular weight of the substance. He has devised an apparatus (Z. physik. Ch. **8**, 223),¹ which renders the measurement of the rise both simple and exact, as well as comparatively rapid. When the solvent has been boiling so long that the mercury column is steady, the temperature is read off, the substance is added, and another reading is made. The addition usually takes place in six or eight portions, and the thermometer is observed after each addition ; the molecular weight is deduced from the data almost as easily as in the case of the freezing-point method.

*Construction and charging of the apparatus.*²—The solution is

¹ Cf. *ibid.* **4**, 543, and **6** 437.

² This apparatus, as well as that used for freezing-point determinations, or any separate parts of either, can be obtained from F. O. R. Götze. Leipzig.

boiled in the tube A, which is of the same shape as that used for freezing-point determinations, and has a small piece of platinum wire fused into the bottom to render the boiling steady. It is two

and a half centimetres in diameter, and is filled for three and a half to four centimetres of its height with garnets or glass beads. The thermometer, which is of the construction described in the last section, passes through a cork in the tube, and has its bulb partially embedded in the garnets. This tube is surrounded by the vapour jacket B, whose construction can be best understood from the figure. The jacket is separated from the tube by a sheath of asbestos paper, α , at the bottom, and a little common asbestos at the top; it is charged with about 20 cc. of the solvent and some chips of porous earthenware, to promote regular boiling. The vessels are provided with the condensing tubes K_1 and K_2 for liquids boiling above 60° ; for low-boiling liquids, such as carbon

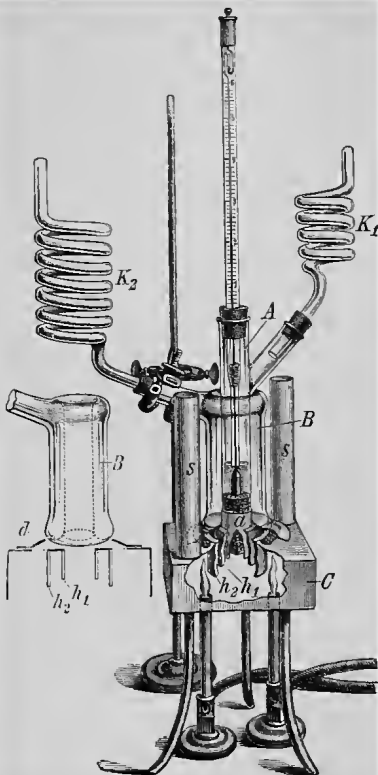


FIG. 31.

disulphide and ether, short light Liebig's condensers take their place. Loosely filled chloride of calcium tubes may be attached to these, when the contents of the vessels are hygroscopic.

Heating.—The heat is distributed by means of an asbestos box C, of peculiar construction, which rests on a tripod stand. Two

small Bunsen flames¹ are arranged corner-wise, so that their heat impinges on an annular opening in the asbestos sheet covered with wire gauze; this is arched over by a ring of asbestos d , which directs the heated air against the jacket. The rings, h_1 and h_2 , are likewise made of asbestos board, and protect the central tube from the direct heat of the flames. Of the solvents mentioned below, water, on account of its high specific and latent heats, is the only one which requires to be heated directly by a third flame; in all other cases the heat from the vapour jacket suffices to keep the solvent in ebullition.

The rate of boiling can be judged very easily by the heating of the condenser tube and by the number of drops per minute which return to the liquid; the heating should be arranged so that one drop falls every five to fifteen seconds, according to the volatility of the solvent.

Boiling-point of the solvent.—As in the case of the freezing-point method, it is not necessary to know the actual temperature of the boiling-point. What is wanted is an exact datum from which to measure the rise; the thermometer, divided into hundredths of a degree described above, is therefore used here also.

As small variations occur in the readings of a thermometer when it is cooled and heated alternately, it is advisable to take the reading always after a rise in the mercury column; as an additional precaution the stem should be tapped with the finger before reading.

When the present form of the apparatus is used, the thermometer shows a constant temperature much more quickly than was the case with the older form; the constancy is recognised by the fact that two readings taken five minutes apart do not differ by more than one or two thousandths of a degree; this does not occur till after the liquid has been boiling from thirty to sixty minutes.

Care should be taken that the chloride of calcium tube does not prevent rapid equalisation of pressure through being partially plugged up, on account of having absorbed much moisture, or for any other cause.

Introduction of the substance.—The substance is introduced through the side tube, the condenser being removed and the boiling momentarily interrupted for the purpose.

For the introduction of liquids, pyknometers, similar to those used

¹ For information about this method and particularly the regulation of the heating, see Sakuri, J. Ch. Soc. **61**, 995

in the freezing-point method, are employed. They are provided with a long capillary (Fig. 32), so that when ether or carbon disulphide is used, they may reach down to the tube containing the solvent through the condenser tube, without the removal of the condenser itself being necessary. They may be graduated into cubic centimetres to facilitate the estimation of the amount introduced. They are filled by suction, the end of the capillary being dipped into the liquid, and a chloride of calcium tube being placed at the other end to prevent access of moisture.

Solid bodies are best introduced in the form of compressed tablets, made by pressing the dry powder in a small machine made for the

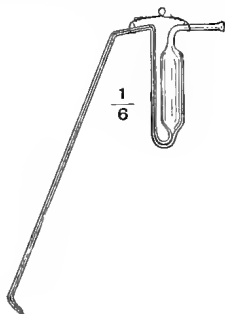


FIG. 32.

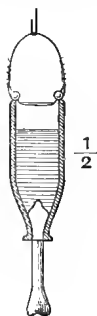


FIG. 33.

purpose, or they may be made into little cylinders by V. Meyer's method (p. 78), when they melt without decomposition.

Both solids and liquids can be introduced in the little tube shown in Fig. 33. It is provided with a valve which opens as soon as the tube touches the garnets. The introduction of vessels of any description, however, should be avoided as much as possible.

Reading of the elevation in the boiling-point.—The introduction and solution of the substance causes a depression of the temperature, but it soon rises again, and becomes constant at a point higher than the original reading. If the ascent of the column lasts more than a minute or two, this must be caused by delay in the solution of the substance. The height of the column is constant when the reading does not vary more than a few thousandths of a degree in from three to four minutes.

It is advisable to make the determination at different concentrations, just as in the case of the freezing-point method. Immediately after the first reading a second quantity of the substance is added, then a third, and even a fourth quantity. 0.1 gr. or so with an elevation of 0.1° may be used to start with, and the amount gradually increased as far as may be convenient.

If more of the substance is added than can be dissolved a slow depression of the mercury column frequently follows the elevation. The solution is at first supersaturated, and then some of the substance is redeposited. In such cases the undissolved part will be found afterwards underneath the beads at the bottom of the tube. The thermometer gives complete information of all that goes on inside the apparatus during the experiment, and although the contents are visible during the entire progress of the experiment direct observation is not of much service.

The barometer-reading.—With the latest perfected form of the apparatus, the time occupied by a determination is so short that no appreciable change in the level of the barometer can take place during its progress. When a long series of determinations is made, however, it will be advisable to check the barometric reading by a second observation.

Completion of the experiment.—When the last thermometer-reading has been made, the heating is interrupted and the apparatus allowed to cool. The progress may be hastened finally by dipping the inner tube in cold water. The condenser is then removed and the tube weighed, as at first, to determine the exact concentration for use in calculation. With careful work the loss of solvent by evaporation need not exceed a few decigrams.

The fraction of the solvent which is removed from the solution by evaporation and condensation in the condenser is greater in the present form of the apparatus than in the older, as the total amount used is less than before. To allow for this Beckmann finds that from 0.15 to 0.2 gr. in case of easily condensed liquids, and about 0.35 gr. in the case of water must be deducted from the amount of the solvent taken.

The substance used can be recovered completely by allowing the solvent to evaporate. To obtain the part adhering to the beads, the latter must be placed in an extraction apparatus, and exhausted with a small quantity of the solvent.

The formula $M = 100 \cdot \frac{G \cdot g}{G(t_1 - t)}$ gives the result directly from the data.

M = the molecular weight,

c = the molecular elevation of the boiling-point for 100 gr. of the solvent,

g = the weight of the substance,

G = the weight of the solvent,

t = the boiling-point of the solvent,

t_1 = the boiling-point of the solution.

Solvent.	Boiling-point.	c .
Acetic acid (glacial) . .	118.1	25.3
Acetone . .	56.3	16.7
Aniline	183.0	32.2
Benzene	80.3	26.7
Carbon disulphide . .	46.2	23.7
Chloroform	61.2	36.6
Ethyl alcohol . . .	78.3	11.5
Ethyl ether	35.0	21.1
Methyl alcohol . . .	66.0	9.2
Phenol	183.0	30.4
Water	100.0	5.2

It may be remarked, in concluding this chapter, that other simple methods of determining the molecular weight are known. That devised by Will and Bredig (Ber. **22**, 1,084 and **25**, 1,401) is worthy of mention.¹ They determine the loss of weight which a solution of the substance under investigation undergoes when a stream of air is drawn through it, all necessary precautions being observed. In order that the air may become thoroughly saturated with the vapour of the solvent, the solution is placed in a sort of Liebig's apparatus provided with nine bulbs instead of the usual three. The numbers obtained show about the same degree of accuracy as those given by Eykman's apparatus.²

¹ They give a complete bibliography of the subject in their first paper.

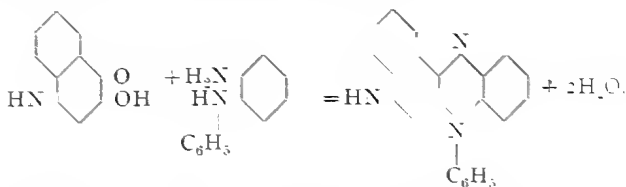
² A new method of determining molecular weights by measuring the "diminution of solubility" of a substance containing a foreign body has been described by Küster, Ber. **27**, 328.

CHAPTER X

SEALED TUBES

1. Reactions in Closed Vessels.—When it is desired to bring about an interaction between two substances at a temperature higher than the boiling-point of one of them, it is necessary in almost all cases¹ to heat them together in a closed vessel. No description is required of the autoclaves which are used on a large scale and the pressure bottles in use in laboratories for this purpose. The details depend on their construction.

As an example of the use of the latter may be mentioned the synthesis of rosininduline by Kehrmann and Messinger (Ber. **24**, 587). Oxynaphthoquinoneimide (5 gr.) was heated with the amount of amidodiphenylamine corresponding to one molecule, acetic acid (5 cc.), and alcohol (300 cc.), in a pressure bottle in boiling water for 48 hours.



Sealed tubes are generally preferred in the laboratory for purposes of this kind.

Sealed tubes can stand a very high pressure without bursting if they are properly handled. Potash glass is preferable to soda glass, but is not absolutely essential. Indeed, the former is not unattacked by water at a high temperature. Hoppe-Seyler (Z. physiolog. Ch. **13**, 73) mentions that he charged a tube 30 cm.

¹ See however Chap. IV. § 4.

long of the best potash glass with water, and heated it for six hours at 180–200°. He found that the interior became covered with a whitish film, and that the water had taken up a small, but perfectly measurable amount of alkali.¹

When solid bodies are in question they are placed in a tube closed at one end, and the other end is then drawn off and sealed.

In the case of liquids the open end is slightly drawn out and the substances are poured in through a thistle-tube with a long narrow stem. It depends entirely on the degree of pressure which is expected what proportion of the whole length of the tube may be filled. In withdrawing the thistle-tube, care must be taken not to touch the part to be fused with the fluid, as this might make the proper sealing an impossibility.

The operation of sealing is conducted in such a way that the end is drawn out into a capillary point, while the tube wall is not allowed to become too thin.

The opening of the tube, after the interaction is complete, must always be conducted with care. The tube must first be completely cold. If volatile substances like methyl chloride may have been formed, the tube should be cooled in ice before opening. If the gases which have been formed are not to be examined, the whole tube, with the exception of the extreme point, is wrapped in a towel; it

then fixed in a clamp and a flame applied to the point. As soon as the glass softens the gases force their way out. If the pressure has not been excessive, none of the other contents of the tube will be carried out with them.

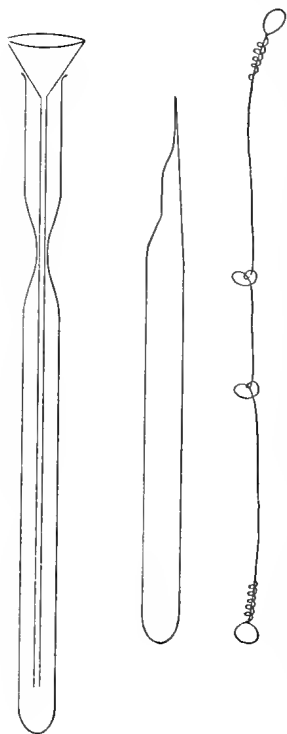


FIG. 34.

¹ See also Ber. **25**, 2,494.

Excessive pressure may be avoided by not adding the whole of the gas-producing substance at once. If, for example, bromine is used and hydrobromic acid is liberated, only one third of the necessary amount may be added at first. Then when the action is complete the tube may be opened, the second third put in, and the tube resealed. The remainder may be added later in like manner. If, on the other hand, the pressure is due to the high temperature employed, it may be advisable to heat at first to 200° only, to cool the tube and let out the gas, and, after resealing, to complete the heating.¹

Städel (Ann. **195**, 190) recommends, as especially applicable in the case of pressure due to hydrobromic acid, filing the tube near the point under water. The tube empties itself without any loss of material through the small opening.

When the product is solid it may be extracted without damage to the tube by filling this with a suitable solvent and inverting it in a wide beaker containing some of the same liquid. As the layer of liquid at the top dissolves the substance it becomes heavier, and, sinking downwards, is replaced by a less nearly saturated portion of the solvent. In a short time the whole is dissolved automatically.

Only one instance seems to be found in chemical literature where the tube was opened while still hot. Einhorn (Ber. **16**, 2,208) says that he warmed 10 grams nitrocinnamic acid with 100 grams of glacial acetic acid saturated with hydrobromic acid at 0° , and that the tube was agitated and the heating continued till solution was complete. As soon as this occurred the tube was opened to prevent the excess of hydrobromic acid destroying the addition product.

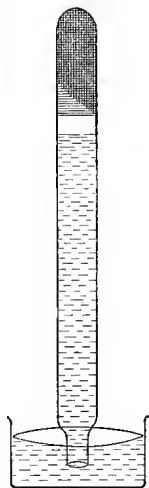


FIG. 35.

2. The Gases in Sealed Tubes.—*If the gases are to be investigated* they are collected in a gasholder of suitable dimensions, and are then conducted through an absorption apparatus, of which the separate parts contain ammoniacal silver solution, dilute hydro-

¹ If a high pressure is wanted and a high temperature must not be used, an indifferent substance of low boiling-point such as ether, acetone, or chloroform may be added.

chloric acid, solution of ferrous sulphate, bromine under water, and solution of potassium or barium hydroxide. In the ammoniacal silver solution such substances as acetylene and allylene produce precipitates which, after drying (the drying must be carried out *in vacuo*), are very explosive. To analyse them a weighed portion is decomposed in a porcelain crucible with hydrochloric acid.

The dilute hydrochloric acid catches ammonia and volatile bases. The bromine is dissolved with cold dilute caustic potash, and any oil which remains undissolved must be an addition product of bromine with an unsaturated body. The baryta water, which can be replaced by an ammoniacal solution of barium chloride, takes up the carbon dioxide. The ferrous sulphate takes up nitric oxide. What passes out unabsorbed can only be investigated fully by a quantitative analysis. Yet it is usually possible to ascertain from the equation what the product is and to identify it by qualitative tests.

Carius (Ann. **169**, 319) has devised the following method for catching the gases when the pressure is high. A graduated glass tube is filled with water, inverted, and a rubber tube pushed up inside it half way to the top. The lower end of the rubber tube is attached firmly to a wide, but rather short, bent tube, with whose second upturned limb another short rubber tube is connected. The end of the sealed tube is pushed firmly into this, so that the capillary reaches into the bent tube itself, and the joint is under the water in the trough. When the point of the capillary is cautiously broken a part of the gaseous and almost all the fluid contents are expelled into the apparatus.

Salkowski (Z. physiolog. Ch. **4**, 464) has given complete instructions for the removal of ammonia from tubes for the purpose of quantitative estimation. This is necessary in cases like the urea determination by Bunsen's method.

If it is desired to *generate chlorine or ammonia* in a sealed tube the following methods may be used:—

For chlorine, hydrochloric acid is added after the tube has received its charge of material. Then a plug of glass wool is inserted, and on the top of that some dry potassium chlorate, potassium bichromate, or manganese dioxide is placed (Ann. **255**, 370). After the tube has been sealed and laid in the oven the development of chlorine begins.

For generating ammonia, ammonio-zinc chloride and bromide mixed with chloride and bromide of ammonium are used. Am-

monio-calcium chloride may also be employed. For example, when *a-m*-xylenol (one part) is mixed with ammonio-zinc bromide and ammonium bromide (one part), and heated at 340° for forty hours, a 25 per cent. yield of xylidine is obtained (Ber. **20**, 1,039). Seyewitz (C. R. **109**, 816), by heating resorcinol $C_6H_4(OH)_2$ with ammonio-calcium chloride for three hours at 300° in a sealed tube converted 60 per cent. of it into metaphenyldiamine.

Ammonio-zinc chloride is made, according to Merz and Müller (Ber. **19**, 2,902), by leading dry ammonia into melted zinc chloride in a retort. The gas is absorbed with evolution of heat, and when the salt is saturated it is allowed to cool in a stream of the gas. Made in this way it is a solid transparent substance which is not deliquescent and has the composition $ZnCl_2 \cdot 2NH_3$. The addition of ammonium chloride is to prevent the formation of zinc oxychloride through the partial decomposition of the chloride, as the presence of this substance would tend to defeat the action. Ammonio-zinc bromide is made in the same way, and has the composition $ZnBr_2 \cdot 2NH_3$. It is hygroscopic, however.

To determine the pressure in a sealed tube, Reychler's method (Ber. **20**, 2,461) may be used. A thin glass tube about 40 cm. long is silvered on the inside for 4 or 5 cm. from one end, bent in the middle, and filled to a certain height with mercury. The silvered end is then sealed hermetically, and the mercury in the open limb covered with a protecting layer of a hydrocarbon. After the length, L , of the enclosed air (A B), the temperature, t , and the barometric pressure, P , have been taken, the tube is let down into the wider tube containing the substance, and the latter is sealed up. The pressure developed in the tube compresses the air in A B, and the mercury column dissolves the silver up to C. After the operation the manometer is withdrawn and the distance A C, (L'), gives the volume of the air at the maximum pressure attained. P' is the pressure in millimetres of mercury in the tube at t' , the temperature of the bath. h' is the vapour tension of mercury expressed in millimetres of mercury, and α is the coefficient of expansion of the gas ($= 0.00367$). The following formula gives the value of P' :

$$P' = \frac{L \cdot P(1 + \alpha t')}{L'(1 + \alpha t)} + h'$$



FIG. 36.

This method is only approximate, as the length L' is sometimes difficult to measure exactly. The silvering must be carefully carried out and the apparatus kept in an inclined, or, better still, vertical position. The result may be checked by experiments carried out in autoclaves, when the gauge attached to the apparatus gives the pressure directly.

3. Experiments on a Small Scale.—Such experiments can be made by Drechsel's very excellent method (J. pr. Ch. **135**, 422).

The tubes generally used for sealing require considerable quantities of material, and much is lost by explosions. By employing ordinary glass tubes 3 or 4 mm. in internal diameter with walls 1 mm. thick, however, preliminary experiments with a few milligrams of the substance can be made. The tube is sealed at one end, charged with the materials, and drawn out at the other end to a very long thin capillary. The tube after being drawn out should not be more than from 5 to 6 cm. long, while the capillary should be from 10 to 15 cm. in length. The tube is fixed in a long wide test tube, and maintained in position by a notched cork, which is split along its length to hold the capillary, so that the lower end is about 1 cm. from the bottom of the outer tube. A liquid of suitable boiling-point is added, so that the tube is covered for half its length by it. The flame which heats the apparatus is regulated so that the vapour plays upon the whole of the tube and part of the capillary, and yet does not reach the cork. The whole is placed in a hood and the window is shut. Explosions seldom occur even with sulphur vapour, and when they do no serious damage can be done. When a general idea of the progress of, and the conditions necessary for, the reaction has been obtained in this way, it is much easier to make proper arrangements for repeating it on a larger scale.

4. The Oven and Accessories.—*Iron tubes enclose the sealed glass tubes* during the heating. A brass wire like that in Fig. 34 is bound round the tube so as to be used in drawing it forth without fear of breakage.

The furnace must have the following qualities according to Babo (Ber. **13**, 1,219).

It must permit of the heating of several tubes of the usual dimensions to a temperature near the boiling-point of mercury, each tube being heated as uniformly as possible.

The measurement of the temperature must be provided for, and the apparatus should be so arranged that a certain maximum cannot be surpassed.

It should be so arranged that if one tube bursts the others may not explode from the shock, and all danger to the experimenter must be avoided.

The expenditure of gas should be as small as possible, and irregularities in its flow should be prevented by proper regulators. Such regulators, it may be mentioned, are also useful in heating air baths and for similar purposes. Victor Meyer (Ber. **17**, 478) recommends Giroud's rheometer, which is made of metal, while Beckmann (Z. physik. Ch. **4**, 546) prefers the Elster membrane-regulator.

The furnace should be placed in a hood so that if an explosion takes place the vapours may be carried off.

Explosions cannot be avoided entirely, and usually the only precautions taken are to secure that they shall do no damage. Yet some efforts have been made to prevent them.

Hittorf, in heating phosphorus and lead together so as to get crystals of the former, embedded the tube in magnesia in an iron tube closed at both ends by screw caps and heated directly in a fire. Bunsen, in his method for determining nitrogen, placed about 0.3 gram of the substance with 5 grams of cupric oxide in a dry tube filled with hydrogen. The tube was put into a mould containing plaster of Paris, and when this was dry the whole was kept at a dull red heat for an hour.

Wöhler (1857, Ann. **103**, 117) heated tubes to 150° in a steam boiler in which a pressure of about five atmospheres was maintained. As his tubes were charged with solutions in water, the pressure outside and inside the tubes was nearly the same, and no explosions were possible.

Ullmann (Ber. **27**, 379) finds that at high temperatures water disintegrates the glass of the tube. He encloses the glass tubes in tubes of steel closed by tightly fitting caps and containing a volatile liquid. The pressure of the latter on the outside of the sealed tube balances the internal pressure and reduces the risk of bursting to a minimum. Furnaces and tubes constructed on this plan are made by Muencke of Berlin.

On account of the inconvenience and risk of explosion and consequent loss of material attaching to work with sealed tubes their use is avoided whenever it is possible. The effort to find

other ways of carrying out chemical actions has frequently been successful. It was supposed, for instance, that splitting off the sulpho-group from aromatic compounds where this could be accomplished at all was only to be attained by heating with hydrochloric acid in sealed tubes. Yet it has been shown by Turner (Ber. **25**, 968) that a good yield of *o*-nitraniline can be obtained by boiling *o*-nitraniline sulphonic acid with three times its weight of 68 per cent. sulphuric acid for half an hour after solution is complete.

CHAPTER XI

SUBLIMATION

“THE sublimation of organic bodies is an operation which must often be used for their purification. In such cases the amount of material at hand is limited, and the losses entailed by re-crystallisation, decolorisation, and similar operations are so considerable that it seems very desirable to reduce these losses to a minimum in order that the thorough examination of such bodies may be facilitated. The apparatus used in sublimation, however, does not usually fulfil this condition, and its many defects are familiar to the chemist.” Thus wrote Gorup-Besanez (*Ann.* **93**, 265) in the year 1855 on sublimation as practised in the laboratory; and while the question has been solved as far as manufacturing chemistry goes, the want of a generally applicable apparatus for use on a small scale is still felt. So far the advantage seems to lie with those designed to work with diminished pressure.

We owe to Kolbe the suggestion of an apparatus for the purpose, consisting of two watch-glasses ground to fit together closely and held in position by a brass clip. A piece of filter paper cut to the size of the glasses is placed between them. Gorup-Besanez recommends heating on an air bath, and controlling the temperature in accordance with the readings of a thermometer (*Fig. 37*). The vapour of the substance is filtered, so to speak, by the paper, and condenses on the highly-arched upper watch-glass, usually in beautifully crystalline form. To cool the upper glass a small piece of netting is placed on it, and ether is dropped cautiously from above.

The paper septum prevents the falling back of the sublimate amongst the residue.

Larger quantities of material are sublimed from a retort, and we owe to Liebig (Ann. **101**, 49) the idea of passing a stream of gas through it to facilitate the operation and remove the sublimate from the danger of decomposition by long exposure to a high temperature. The use of an indifferent gas in this way was found in fact to effect a great improvement in the yield. By the use of a stream of carbonic acid he got, for example, more than 80 per cent. of the theoretical yield of pyrogallic acid from gallic acid.

Baeyer (Ann. **202**, 164) used a different method for very difficultly volatile substances. The bottom of a small wide beaker was covered with the substance. A glass tripod stand with short legs was placed in the beaker, and on this rested a disc of filter paper touching the sides all round. Another disc of filter paper, covered by a funnel, rested on the top of the beaker. Through the stem of the funnel, and through the filters, passed a glass tube which reached almost to the bottom of the vessel. The beaker was heated strongly on a sand bath, and during the heating a rapid current of carbonic acid was led through the tube. At the close of the operation the substance was found between the filter papers and on the inside of the funnel.

Schützenberger places not more than 1 gram of the dry substance in a wide porcelain crucible about 5 or 6 cm. high.

This is covered with a filter paper, the lid is placed over the whole, and the apparatus heated on a sand bath. Fischer (Ber. **22**, 357) recommends the same method.

Another way consists in spreading the substance on the floor of an Erlenmeyer flask and immersing this, along with a thermometer, about 1 cm. deep in a sulphuric acid bath. When the sublimate ceases to increase in quantity, the flask is removed from

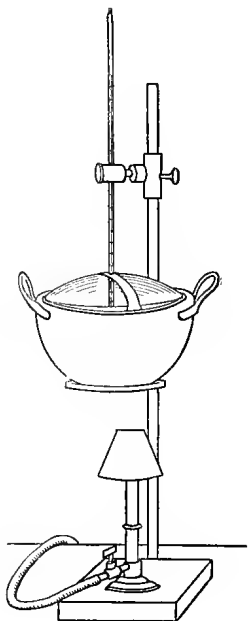


FIG. 37.

the bath, and, if necessary, the bottom can be cracked off to separate the sublimate from the residue.

Tollens (Ber. **15**, 1,830) sublimed trimethylene oxide 1 gram at a time by placing it in a sealed tube, and packing this in the steel tube of a Carius furnace with asbestos, so that the part containing the substance was in the furnace and the empty half projected. He then raised the temperature to 180–185°.

Brühl and Landolt have contrived arrangements in which cooling by water plays a part.

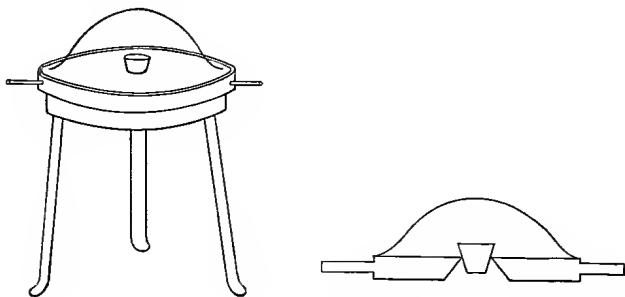


FIG. 38.

Brühl's apparatus (Ber. **22**, 238), which is specially suitable for easily fusible sublimates, consists of a tripod stand surmounted by a low disc shaped tin box. A conical opening in the centre holds a crucible, and two attachments for leading water through the box are provided at opposite sides. This cooling arrangement is covered by a glass basin with ground edge. The crucible should be long in form and made of a good conductor such as copper or platinum. The original form of the apparatus may be improved by covering the tin box with a plate of glass, perforated in the middle, which precludes contact of the sublimate with the metal of the cooler. If the basin is rather high, almost all the sublimate will be deposited on the cooled glass plate.

The apparatus can be used for fractional sublimation also.

Landolt's (Ber. **18**, 57) arrangement for sublimation consists of a tube of thin platinum foil about 150 mm. long and 18 mm. wide. It is closed at the bottom, and two glass tubes traverse the stopper at the top. Water enters by the longer of the two, which reaches

almost to the bottom, and finds an exit by the other. The apparatus is let down into a wide-necked flask in which the substance is heated, and the substance deposits itself on the cold surface, and so can be easily withdrawn and scraped off.

When difficultly volatile substances are heated in a platinum or porcelain crucible, a screen of tin plate or asbestos board must be provided to protect the projecting part of the tube, as otherwise a considerable amount of water may condense upon it.

Success has not attended efforts to replace the platinum tube by a glass test tube.

Very recently Hertkorn (Ch. Z. **1892**, 795) has described still another form of laboratory sublimation apparatus.

Sublimation in vacuo was probably first used by Sommaruga (Ann. **195**, 305). After vain attempts to purify indigo by sublimation without decomposition, he finally placed it in flasks of about 80 cc. capacity, and reduced the pressure of air in them to 30-40 mm. By direct heating he could then obtain any desired quantity of the sublimate in a short time.

Volhard (Ann. **261**, 380) placed crude pyromucic acid between two plugs of asbestos in a glass tube which was then heated in an air bath. The one end of the tube was connected through a receiver with the pump; at the other was a tube provided with a screw clip through which dry air could enter. With a pressure of 50-60 mm. the acid sublimed in long white needles at 130-140°.

In a similar manner Bourgeois sublimed urea in vacuo, by the use of a mercury bath heated to 120-130°. Thiourea when treated in the same way was converted into ammonium sulphocyanate. The employment of a mercury bath does not seem desirable, however, on account of the poisonous nature of the fumes arising from it.

PART II

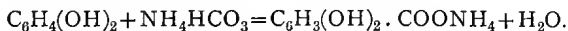
SPECIAL METHODS

CHAPTER XII

CONDENSATION

1. General Remarks.—By condensation we mean the formation of a substance from two others with loss of water, alcohol, hydrochloric acid, ammonia, or a halogen from both components.

The union may take place without the addition of any condensing agent, as in the case of the action of hydroxylamine, and phenylhydrazine on aldehydes and ketones. Senhofer and Brunner (Z. physiolog. Ch. **2**, 22) found, for example, that polyatomic phenols (*e.g.* resorcinol), interact directly with ammonium carbonate dissolved in water and produce carboxylic acids.

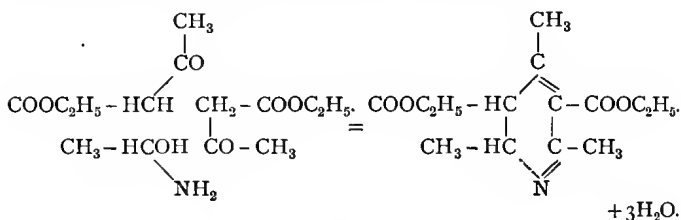


In most cases however the tendency to condensation is strengthened by the addition of suitable agents.

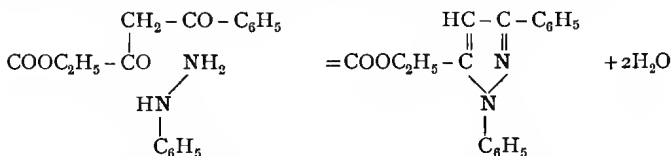
We include under this heading also the phenomenon of internal condensation in which a body loses water, and forms a new substance. Thus diacetosuccinic acid is transformed into carbopyrotritic acid in presence of phosphoric acid (Ber. **17**, 2,863).

When substances condense with themselves without loss of water, the process is called polymerisation,

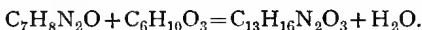
By means of condensation chemists have been able to prepare far more new bodies and entire classes of bodies than by any other process. With its help also the transformation of substances constituted with open chains into those with closed chains has been vastly simplified. As an example of the latter, Hantzsch's synthesis of pyridine derivatives (Ann. **215**, 74) may be mentioned. Thus he obtained hydrocollidine dicarboxylic ether by the union of two molecules of acetoacetic ether with one molecule of aldehyde ammonia, and loss of three molecules of water.



Another example similar to this is afforded by Beyer and Claisen's (Ber. **20**, 2,186) preparation of diphenylpyrazol carboxylic ether by the action of phenylhydrazine on benzoylpyruvic ether :



In most cases condensations can be carried out in open vessels, and the use of sealed tubes is seldom necessary. An instance where this is necessary is reported by Behrend (Ann. **233**, 2). He found that phenylurea and acetoacetic ether in alcoholic solution did not combine even in presence of hydrochloric acid. Even heating to the boiling-point of acetoacetic ether did not bring about the desired result. But the interaction was easily induced by heating phenylurea (10 gr.), acetoacetic ether (20 gr.), and ether (10 cc.) for six hours at 140–150°. The yield was equal to 90 per cent. of the theoretical.



It is hardly necessary to point out that the formation of esters,

and ethers is only a special case of condensation. It is treated in a separate chapter for the sake of convenience.

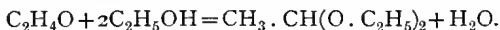
2. Condensing Agents.—The following are the chief agents used for bringing about condensation.¹ They are arranged alphabetically, and will be discussed in detail in the order given.

Acetic acid.	Phosphorus pentoxide.
Acetic anhydride.	Phosphorus trichloride.
Aluminium chloride.	Potassium bisulphate.
Ammonia.	Potassium cyanide.
Antimony trichloride.	Potassium hydroxide.
Barium hydroxide.	Silicic ether.
Benzotrichloride.	Silver.
Boron trifluoride.	Sodium.
Calcium chloride.	Sodium acetate.
Calcium hydroxide.	Sodium ethylate.
Copper.	Sodium hydroxide.
Hydrochloric acid.	Sulphur.
Hydrocyanic acid.	Sulphuric acid.
Magnesium chloride.	Tin tetrachloride.
Oxalic acid.	Zinc.
Perchloroformic ether.	Zinc chloride.
Phosgene.	Zinc dust.
Phosphorus oxychloride.	Zinc oxide.

It must be emphasised that one condensing agent cannot, as a rule, take the place of another ; indeed, in cases where equivalence might *à priori* be assumed, it is often found that quite divergent results are obtained, especially in respect to yields. Thus Baeyer (Ber. **6**, 223) found aldehydes and hydrocarbons are not always satisfactorily condensed by sulphuric acid or a mixture of that with glacial acetic acid. Griepentrog (Ber. **19**, 1,876), on the other hand, found that zinc chloride almost invariably gave good results. In this connection also the behaviour of oxalic acid (§ 17) may be cited.

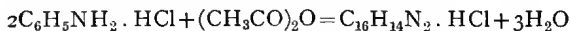
¹ The extraordinary effect of sunlight in causing condensation has been investigated by Klinger. Klinger and Standke (Ber. **24**, 1 340) found that sunlight could with extreme ease induce the formation of substances which could only be obtained in its absence by very powerful or very subtle chemical means.

3. Acetic Acid.—Acetic acid can be used for promoting the condensation of aldehydes and alcohols to acetals.



Thus Geuther (Ann. **126**, 65) prepared acetal by allowing alcohol (6 vols.), aldehyde (2 vols.), and glacial acetic acid (1 vol.) to stand in a sealed tube for eight days and then heating the mixture at 100° for twelve hours.

4. Acetic Anhydride.—The use of this substance is almost confined to Perkin's synthesis. Baum heated aniline hydrochloride (12 parts) with acetic anhydride (18 parts) for twelve hours at $180-200^\circ$. The action took place according to the equation—

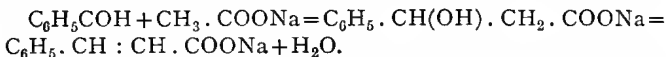


without previous formation of acetanilide. A part of the acetic anhydride acted as a condensing agent.

The discovery of Perkin's synthesis (J. Ch. Soc. **31**, 391) led to the opening of a wide field for the use of acetic anhydride.

Perkin prepared cinnamic acid by heating benzaldehyde (2 parts), sodium acetate (1 part), and acetic anhydride (3 parts). Tiemann and Herzfeld (Ber. **10**, 68) used the proportions, benzaldehyde (3 parts), pulverised acetate (3 parts), and acetic anhydride (10 parts), and boiled the mixture in a flask, provided with a condensing tube, for eight hours. When the mass is extracted with water an oil remains which is dissolved in ether. Any unused benzaldehyde is removed by shaking with sodium bisulphite, and then the cinnamic acid is extracted with a solution of sodium carbonate. On acidifying the solution with hydrochloric acid the organic acid is precipitated.

Fittig has shown (Ber. **14**, 1,826) that combination first occurs between the aldehyde and the sodium salt, and then the acetic anhydride removes the water.



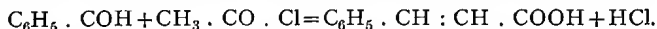
Cumarin (J. Ch. Soc. **31**, 389) is formed by boiling salicylic aldehyde with acetic anhydride and sodium acetate. By using different aldehydes different acids are obtained, and homologues are formed by using homologues of sodium acetate in place of the simple acetate.

The yields obtained by the use of Perkin's synthesis lie usually

between 40 and 50 per cent., but often sink below this level when there is opportunity for secondary reactions.

It may be worth mentioning that Plöchl and Wolfrum (Ber. **18**, 1,183) heated hippuric acid (1 mol.) and salicylic aldehyde (1 mol.) with three times their weight of acetic anhydride and half their weight of sodium acetate on the water bath. The condensation took place exclusively between the first two substances, and not a trace of cumarin was found.

Edeleano and Budistheano (Bull. Ch. [3], **3**, 191) have combined Perkin's synthesis with an old observation of Bertagnini's. The latter obtained cinnamic acid by the action of benzaldehyde on acetyl chloride (Ann. **100**, 126)—



Now the former observers found that by boiling benzaldehyde (1 mol.), acetyl chloride (1 mol.), and sodium acetate (3 mol.), for twenty-four hours an almost quantitative yield of cinnamic acid was obtainable. If this is literally true, the very favourable result may be due to the acetic anhydride, formed from the two last ingredients, acting, so to speak, *in statu nascendi*.

5. Aluminium Chloride.—We owe the use of aluminium chloride for synthetical purposes to the work of Friedel and Crafts (Bull. Ch. **29**, 2). As Baeyer has remarked, this method has been so fruitful and so varied in its results that an account of them reminds one of a fairy tale. If we include with this the zinc chloride method we have here certainly far the most prolific of all the modern synthetical methods. It has brought to our knowledge whole classes of bodies of the most diverse kinds.

The theory of the action is even now not perfectly settled, as is shown by some recent work of Gustavson (J. Ch. Soc. **60**, 182).

The chloride freshly prepared from aluminium and chlorine usually gives better results than the frequently impure commercial article (cf. however Biltz, Ber. **26**, 1,960). It melts at 194° (Ber. **24**, 2,577). Stockhausen and Gattermann (Ber. **25**, 3,521) give the following directions for preparing it. A wide combustion tube of infusible glass, drawn out at one end to a narrower tube, is connected with a wide-mouthed bottle by a doubly perforated cork. A sufficiently wide tube passes through the other hole and conducts escaping fumes to the draught. The combustion tube is filled with aluminium turnings, placed in a furnace, and dry hydrochloric acid gas is led through it. When all the air has been driven out of the apparatus

and there is no danger of an explosive mixture being formed, the metal is heated to a temperature such that it will not melt into drops. The chloride then distils into the bottle, whose cork must be protected with asbestos paper to prevent its being burned during the process. The yield is four parts of chloride from each part of the metal taken.

According to Anschütz (Ann. **235**, 154), actions involving the use of aluminium chloride are best carried out in a rather large round-bottomed flask attached by a tubulated adapter to an inverted condenser (Fig. 10). The chloride can be introduced through the tubulus, which can serve also for the introduction of a thermometer showing the temperature of the liquid during the operation. The action can be promoted by warming in a water bath if necessary, and when hydrochloric acid ceases to be evolved, the product is poured into water and extracted with benzene, ether, or other suitable medium.

The yields are frequently unsatisfactory, and vary very greatly when different classes of substances are compared. Thus better yields are obtained with homologues of benzene than with benzene itself, while with aromatic halogen derivatives the opposite is true (Schöpf, Ber. **24**, 3,766).

Possibly the occurrence of bad yields may be ascribed to the fact that the action of the chloride on undiluted substances is too violent and leads to the formation of resins. To test this, Claus and Wollner (Ber. **18**, 1,856) placed 100 grams of the chloride in a flask provided with a condenser, and covered it completely with *carbon disulphide*. Then they added a mixture of *p*-xylene (100 gr.) and acetyl chloride (75 gr.) in small portions at the ordinary temperature. The operation was interrupted at the end of an hour and a half, although hydrochloric acid was still being evolved, because resinous matter was seen to be forming. The mass was poured into water and the mixture extracted with ether. *p*-xylylmethylketone (60 gr.) was obtained from the extract.

With the same object in view, Elbs (J. pr. Ch. **141**, 181) mixed hydrocarbons with acid chlorides in molecular proportions, and added enough carbon disulphide to produce a clear solution.

All vessels used for syntheses by this method must first be well dried. Then an amount of carbon disulphide equal in volume to the mixture of substances to be combined is placed in the flask and about the same quantity of aluminium chloride is added. The mixture is then poured through the adapter in portions, an interval

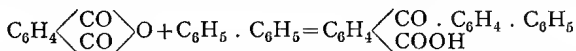
elapsing between each addition to permit the violence of the action to abate. When the whole has been added, the mass is warmed in the water bath until the evolution of hydrochloric acid has ceased. When the mixture has cooled a little water is added and the whole is agitated. This process is repeated as long as any fresh action is visible, and finally the product is distilled in a current of steam. Ketones of high molecular weight remain in the residue as heavy oils, with a solution of aluminium chloride floating on the top. The ketones are washed with very dilute hydrochloric acid, to free them from alumina, and purified by distillation. The yield of the pure products reaches 50–80 per cent. of the theoretical.

Elbs ascribes the usefulness of the carbon disulphide to three causes. In the first place it dilutes the substances and ensures quicker action. Secondly, it keeps the temperature during the operation at 50°, a height which seems to be generally favourable. And, finally, it moderates the violent action of the water on the product and prevents the formation of resin. This last property he holds to be especially valuable.

The quantity of aluminium chloride can frequently be diminished to one half the weight of the acid chloride used without interfering with the yield. The time necessary for the completion of the action varies from a half to two days.

The following actions differ somewhat from those cited. Gattermann (Ann. **244**, 50) acted with carbamic chloride, $\text{NH}_2 \cdot \text{CO} \cdot \text{Cl}$, on benzene in presence of powdered aluminium chloride, using carbon disulphide for dilution, and obtained a quantitative yield of benzamide. Gottschalk (Ber. **22**, 1,219) dissolved pentamethylbenzene (20 gr.) in carbon disulphide (60 gr.), and added first carbamic chloride (20 gr.) and then, gradually, aluminium chloride (24 gr.). The mixture was warmed for a short time in the water bath, and 80 per cent. of the theoretical amount of the amide of pentamethylbenzoic acid was formed.

Elbs (J. pr. Ch. **149**, 147) finds that for some purposes the boiling-point of carbon disulphide is too low, and recommends for such cases the use of *petroleum ether*. Thus, for the formation of phenylbenzoyl-*o*-benzoic acid from diphenyl and phthalic anhydride



the most favourable temperature is 90–100°, so that petroleum ether of this boiling-point is the best diluent to use.

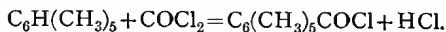
The method usually works well with benzene and its homologues, but is less satisfactory with more complicated aromatic hydrocarbons, and sometimes fails entirely. Substances with halogen atoms attached to the ring act poorly, while nitro-bodies hardly act at all. The method cannot be employed with compounds containing hydroxyl, since the chloride interacts directly with this.

Gaseous substances are amenable to its influence. Thus, by conducting sulphur dioxide (Jahresb. **1878**, 739) into benzene containing the chloride, addition takes place, and benzene sulphinic acid, $C_6H_5SO_2H$, is formed. By using oxygen in place of sulphur dioxide (Ann. Ch. Ph. [**6**], **14**, 433), phenol is obtained.

Galle (Ber. **16**, 1,744) found that for introducing ethyl groups into benzene it was preferable to employ the liquid ethyl bromide rather than the gaseous chloride. The mixture was heated in a tube at 100° . Tetraethylbenzene was the chief product after nine hours' heating, while after fifteen hours the greater part of the benzene had been converted into hexaethylbenzene.

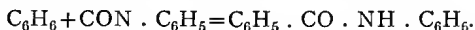
Acid radicals can be introduced in the same way as alkyl radicals. Doebner and Wolff (Ber. **12**, 661) even prepared dibenzoyl quinol (C_6H_5CO)₂ $C_6H_2(OH)_2$ by heating quinol dibenzoate (1 mol.) with benzoyl chloride (2 mol.) in a flask at $190-200^\circ$, and gradually adding aluminium chloride. The quinol had to be used in the form of an ester to avoid the direct action of the condensing agent on the hydroxyl. After the operation had gone on for forty-eight hours, fresh addition of the chloride produced no new evolution of hydrochloric acid. The ester was finally saponified with alcoholic caustic potash, and the product precipitated with carbon dioxide.

Jacobsen (Ber. **22**, 1,220) mixed phosgene (50 gr.) cooled to 10° , and pentamethylbenzene (70 gr.), added gradually aluminium chloride (5-10 gr.), and allowed the whole to remain at a temperature not exceeding 0° for two weeks. The liquid was then exposed to moist air in shallow basins for a short time, and finally warmed with water and caustic soda. The latter converted the chloride into the sodium salt of the acid. A small amount of unused pentamethylbenzene was removed and a good yield of pentamethylbenzoic acid obtained by precipitation with hydrochloric acid.



Phenyl cyanate unites with hydrocarbons in presence of aluminium chloride, forming an acid anilide, from which, by hydro-

lysing, the corresponding aromatic acid is obtainable (J. pr. Ch. **149**, 301).



This action is exceptional in the sense that no hydrochloric acid is evolved.

The acetyl group can be united to the benzene ring by this agency. Thus Schweitzer (Ber. **24**, 550) diluted bromobenzene and acetyl chloride with carbon disulphide and by the usual process obtained acetylbromobenzene, $\text{C}_6\text{H}_4\text{Br} \cdot \text{CO} \cdot \text{CH}_3$, after three hours' heating.

Even inorganic chlorides can be induced to unite with organic radicals. For example, Michaelis and Schenk (Ann. **260**, 2) mixed phosphorus trichloride (100 gr.) with dimethylaniline (70 gr.) and added fresh aluminium chloride (20 gr.) in small portions at once. The mixture was cooled during the process. Dimethylamidophenylphosphine dichloride was formed according to the equation—



In making acetovanillone, Otto (Ber. **24**, 2,869) departed somewhat from the ordinary course. He cooled a solution of pure guaiacol (60 parts) in glacial acetic acid (120 parts), and added gradually a finely pulverised mixture of aluminium and zinc chlorides. He finally heated the mixture at $140\text{--}150^\circ$, keeping the temperature constant between these limits. Even thus, however, the yield was unsatisfactory.

Those examples give some idea of the wide applicability of this synthetical method. It must be said, however, that the action sometimes takes the opposite course. Thus along with actions like



those of the opposite nature

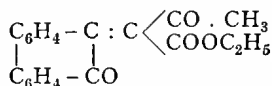


likewise occur. This was shown by Jacobsen (Ber. **18**, 339), who heated hexamethylbenzene with one tenth of its weight of aluminium chloride in a stream of dry hydrochloric acid gas, at a temperature near to its melting-point. He obtained pentamethylbenzene, durene, and even benzene. More remarkable still was the observation of Anschütz and Immendorff (Ber. **18**, 657), that (*e.g.*) toluene

gave both benzene and *m*-xylene and *p*-xylene under the same circumstances (cf. Chap. XXI. § 9).¹

6. Ammonia.—Like other alkaline solutions, ammonia shows condensing properties. It may be remarked here, however, that sodium hydroxide seems to be the most energetic member of the group, and is therefore the most frequently used alkali.

The following case of the use of ammonia is reported by Japp and Streatfield (Ber. **16**, 276). When phenanthrenequinone, acetoacetic ether, and concentrated ammonia are heated at 100° for a short time under pressure, phenanthroxylene-acetoacetic ether



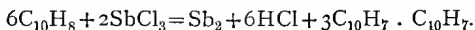
is formed. As the authors remark, this seems to be the first occasion on which the somewhat unusual dehydrating influence of aqueous ammonia has been noticed.

The same influence seems to be specially helpful in assisting the addition of hydrocyanic acid to aldehyde and ketone groups. Thus Kiliani (Ber. **21**, 916, and **22**, 370) found that the addition product with arabinose took eight days for its formation under ordinary circumstances, while the addition of four drops of ammonia for every 100 grams of arabinose diminished the time to from twelve to twenty-four hours. The same observation was made in the case of galactose carboxylic acid. In preparing the cyanhydrine he added water (6 cc.) to finely pulverised galactose (30 gr.), and then the calculated amount of 50 per cent. hydrocyanic acid with one drop of ammonia. The mixture became gradually solid and was filtered after twelve hours. The crystals consisted of the amide of galactose carboxylic acid, and the quantity was equal to 40–50 per cent. of the sugar taken.

7. Antimony Trichloride.—Smith (Ber. **9**, 467) states that antimony trichloride can be used for increasing the yields of hydrocarbons obtained by condensation. Thus, when naphthalene is conducted through red-hot tubes, a very small amount of isodi-

¹ Kondakoff (J. pr. Ch. **156** 467) has recently classified the cases in which aluminium chloride and zinc chloride respectively give the best results. He finds that the former is in general most advantageously used with aromatic bodies, and the latter with fatty derivatives.

naphthyl, $C_{10}H_7 \cdot C_{10}H_7$, is formed. But when the vapour of antimony chloride is passed through at the same time, hydrochloric acid is formed, and a large yield of the condensation product is obtained.



Tin tetrachloride seems to be even more efficient in such cases, as it is transformed into the dichloride, but chloro-derivatives appear always to be formed at the same time. A large amount of diphenyl can be obtained from benzene by its means.

8. Barium Hydroxide.—Böttger (Ann. **172**, 241) found that pyruvic acid could be condensed by means of barium hydroxide. He mixed pyruvic acid (5 parts) with the crystallised hydroxide (3 parts) and enough water to produce a mixture boiling at 140° (Ann. **208**, 126). The products were methylsuccinic acid and pyrotri-tartaric acid.

9. Benzotrichloride.—Wittenberg (J. pr. Ch. **134**, 67) found that resocyanin, $C_{21}H_{18}O_6$ (J. pr. Ch. **132**, 126), could be obtained from resorcinol and acetoacetic ether in presence of benzotrichloride. Still he found that concentrated sulphuric acid gave a better yield.

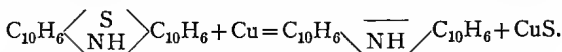
10. Boron Trifluoride.—This substance, which is prepared by the action of sulphuric acid on a mixture of fused and pulverised boric acid with calcium fluoride, has special powers of bringing about internal condensation (Landolph, Ber. **12**, 1,579). Thus it transforms camphor into cymene. It is capable, however, of forming compounds directly with aldehydes, ketones, and probably amines.

11. Calcium Chloride.—This agent is not employed alone, but is frequently used with zinc chloride (cf. § 36).

12. Calcium Hydroxide.—Löw obtained formose, $C_6H_{12}O_6$, by polymerisation of formaldehyde, CH_2O , by shaking a 3.5-4 per cent. solution of the aldehyde with excess of lime-water for half an hour and then filtering. In the course of six days the liquid acquired an intense power of reducing Fehling's solution. The solution was neutralised with oxalic acid, and the calcium formate precipitated with alcohol. The filtrate was then evaporated to a syrup, and the sugar precipitated as a plastic mass by addition of alcohol and ether.

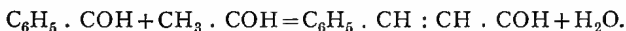
13. Copper.—This metal brings about condensation by removing sulphur and so permitting the union of the organic groups attached to it. It is used in a finely-divided state : probably that prepared by Gattermann's method (Chap. XVI., sec. II., § 13), will be found very suitable for the purpose when dried in a stream of hydrogen or illuminating gas.

Its use may be exemplified by reference to an application made by Ris (Ber. **19**, 2,243). He thoroughly mixed thio- β -dinaphthylamine (1 part) with copper (2 parts), which was freshly ignited in a stream of hydrogen just before use, and heated the mixture in a retort in a stream of carbon dioxide ; soon the metal became black and a yield of fifty per cent. of β -dinaphthylcarbazole distilled over.



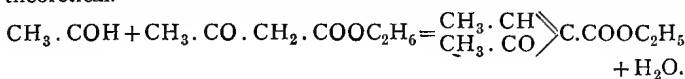
The attempt to unite two different hydrocarbon groups by this agency seems not to have been made as yet.

14. Hydrochloric Acid.—Hydrochloric acid, which is the agent most generally used in the preparation of esters, was probably first employed successfully for the removal of water in other directions by Chiozza in 1856. He conducted the gas into a mixture of aldehyde and benzaldehyde to saturation, noticed the cloudiness due to the separation of water, and isolated cinnamic aldehyde from the product.



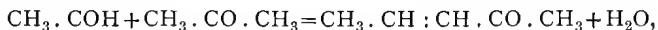
This method is still in use in the same form. The amount of water produced is sometimes measured by placing the mixture in a burette and allowing the water to collect on the surface.

Claisen (Ann. **218**, 172) obtained ethylidene acetoacetic ether by saturating a mixture of aldehyde (1 part) and acetoacetic ether, placed in a freezing mixture, with hydrochloric acid. The material increased in weight forty-three per cent. At the end of twenty-four hours he poured the liquid into water ; the oil which separated was washed with water and carbonate of soda, and finally dried with calcium chloride. On distilling the result he found that much hydrochloric acid came off through the decomposition of an addition product, and then the condensation product, boiling at 210° , passed over. The yield was equal to seventy or eighty per cent. of the theoretical.



Beyer's synthesis of homologues of quinoline (Ber. **20**, 1,767) likewise depends on the condensation of primary aromatic amines with unsaturated ketones, or with mixtures of ketones and aldehydes, by means of hydrochloric acid. He obtained α - γ -dimethylquinoline (J. pr. Ch. **141**, 401) by the following process.

He took paraldehyde and acetone in the proportions required by the equation—

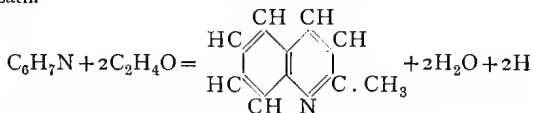


using a small excess of acetone, saturated the cooled mixture with dry hydrochloric acid, and allowed the mixture to remain for one or two days. He then poured it slowly into a solution of aniline in twice its weight of concentrated hydrochloric acid. A little less than the amount of aniline required by the equation was taken and the whole was warmed for several hours in the water bath. A good yield of the base was obtained from the proportions—paraldehyde (120 gr.), acetone (200 gr.), aniline (200 gr.), and concentrated hydrochloric acid (400 gr.). The principal part of the action is represented by the equation—



In isolating the product the liquid is first distilled in a current of steam to remove volatile substances. On then adding excess of caustic soda the basic constituents can be driven off. The bases are dissolved in alcohol, and the picrate of dimethylquinoline is precipitated by adding an alcoholic solution of picric acid. The crystals are washed with alcohol and decomposed with caustic soda, when the free base can be driven over with steam and thus obtained in a pure condition.

In the same way Doebner and Miller (Ber. **16**, 2,465) found that quinaldine could be prepared in a few hours by warming a mixture of paraldehyde ($1\frac{1}{2}$ parts), aniline (1 part), and crude hydrochloric acid (2 parts), on the water bath.

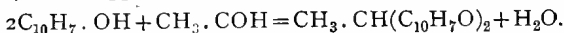


The nascent hydrogen acts upon a part of the quinaldine.

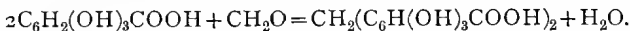
One of the methods of preparing the soporific, sulphonal, depends on the condensation of acetone with mercaptan to mercaptol by means of hydrochloric acid, when oxidation of the product gives sulphonal.

When solid substances are to be condensed, they are dissolved in alcohol, provided this solvent will not affect the action, or, still better, in glacial acetic acid; the actual use of gaseous hydrochloric acid is not always essential, the addition of a few drops of the aqueous acid sometimes suffices.

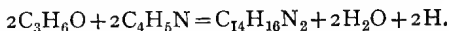
Claisen (Ann. **237**, 271) supplies an example of this. He dissolved β -naphthol (7 parts) and paraldehyd (3 parts) in glacial acetic acid (15 parts), added fuming hydrochloric acid (1 part), and warmed the whole in the water bath. Ethylidene-glycoldi-naphthylacetal appeared as an oil which soon crystallised.



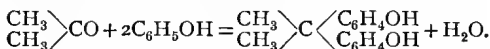
Similarly Caro (Ber. **25**, 946) found that hexoxydiphenylmethane dicarboxylic acid was extremely easily formed by boiling gallic acid (2 mol.) and formaldehyde (1 mol.) with fifteen times as much dilute hydrochloric acid (1 : 5) on the water bath till the substance had completely separated as a white powder.



Condensations similar to these occur also in the pyrrole series. Baeyer (Ber. **19**, 2, 184) states that when pyrrole (1 part) is dissolved in pure acetone (10 parts), and one drop of hydrochloric acid is added, the liquid becomes coloured and soon begins to boil; if it is cooled rapidly crystals of a substance having the composition $C_{14}H_{16}N_2$ appear.



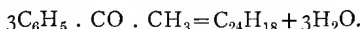
According to Dianin (J. Ch. Soc. **64**, i. 214), fatty ketones condense with phenol to form diatomic phenols. The most favourable temperature for the action is 40–60°. The larger the amount of hydrochloric acid, and the smaller the molecular weight of the ketone, the more quickly is the condensation accomplished. Beyond a certain limit, however, excess of the acid acts disadvantageously. In preparing dimethyl-*p*-diphenolmethane he mixed acetone (220 gr.), phenol (1,600 gr.), glacial acetic acid (1,800 cc.), and fuming hydrochloric acid of sp. gr. 1.19 (600 cc.), and allowed the liquid to remain at a temperature of 40–60°. At the end of twenty-four hours he cooled the mixture, separated the crystals, and set it aside again at the same temperature. In this case he found that heating in a sealed tube at 80–90° completed the action in two days.



The following example illustrates the use of alcohol for diluting. Tetramethyldiamidobenzhydrol (5 parts) is dissolved in hydrochloric acid of

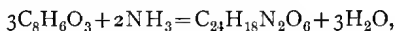
sp. gr. 1.18 (3.5 parts), and alcohol (20 parts) and dibenzaniline (5 parts) are added. The mixture is heated in the water bath until the hydrol has disappeared, and is then diluted with water and filtered. The leuco base is finally precipitated by the addition of water.

Hydrochloric acid is also efficient in promoting internal condensation. Thus Engler and Berthold (Ber. **7**, 1,123) find that acetophenone absorbs dry hydrochloric acid rapidly. After the saturated substance has remained for several days in a warm place crystals of triphenylbenzene appear; by repeating the process sixty per cent. of the acetophenone can be finally converted into the new body—



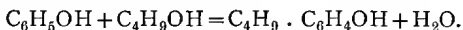
Wurtz (C. R. **74**, 1,361) obtained aldol by the action of hydrochloric acid on aldehyde.¹ He failed however to condense formaldehyde by this method (Bull. Ch. **31**, 434). The polymerisation of the substance to formose, $\text{C}_6\text{H}_{12}\text{O}_6$ (Ber. **23**, 2,126), which is interesting on account of the relation of the latter to the carbohydrates, was achieved by Löw (J. pr. Ch. **141**, 327) by the use of calcium hydroxide (cf. § 12).

15. Hydrocyanic Acid.—Lorenz (Ber. **14**, 791) states that piperonal and alcoholic ammonia condense differently in presence of hydrocyanic acid and in its absence; in the former case the action is represented by the equation—



and the product melts at 213° . In the latter case the substance produced has the same empirical formula, but melts at 172° , and differs from its isomer in other respects as well; it may be that the difference between the substances is stereo-chemical. It is not known whether hydrocyanic acid has any special influence on the course of other condensations or not.

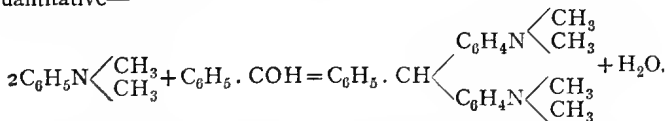
16. Magnesium Chloride.—By the action of phenol on isobutyl alcohol in presence of magnesium chloride, Mazzara (J. Ch. Soc. **42**, 838) obtained isobutylphenol—



17. Oxalic Acid.—Anhydrous oxalic acid was used by Girard and De Laire (Jahresb. **1867**, 963) for preparing diphenylamine—

¹ His work was suggested by the theoretical speculations of Baeyer's paper on "The Role of Condensation in Plant Life" (Ber. **3**, 68).

blue from diphenylamine. In this particular case, however, the acid is itself decomposed. Anschütz (Ber. **17**, 1,078) used dry oxalic acid in making tetramethyldiamidotriphenylmethane. He added pulverised anhydrous oxalic acid (7.5 gr.) to a solution of benzaldehyde (5 gr.) in dimethylaniline (11.5 gr.), and heated the mixture, with constant stirring, for two hours at 110°. The yield was almost quantitative—



After the publication of this, Fischer (Ber. **17**, 1,893) stated that it had been well known to manufacturers ever since the discovery of malachite-green, which is formed by the oxidation of the above derivative, that the condensation of diethylaniline with benzaldehyde is much less satisfactory than that of dimethylaniline when zinc chloride is used as the condensing agent. Indeed it is almost impossible to obtain the diethyl derivative in a crystalline condition when zinc chloride is used in its preparation. So that both for the preparation of the leuco base of malachite-green and the corresponding ethyl derivative, other condensing agents had long been in use. One of these was oxalic acid, which Anschütz first employed in the laboratory.

The presence of other groups in place of hydrogen in the benzene ring does not interfere with the efficiency of this agent. Thus when a mixture of *o*-nitrobenzaldehyde (1 part), diethylaniline (3-4 parts), and oxalic acid (1½ parts), is heated in the water bath, an excellent yield of *o*-nitrophenyl-tetraethyl-*p*-amidodiphenylmethane is obtained.

When resorcinol (7 gr.), phthalic anhydride (5 gr.), and oxalic acid (3.5 gr.), are heated for ten hours, fluoresceine (2.3 gr.) is formed (Ber. **17**, 1,079).

Kaeswurm (Ber. **19**, 744) showed that *p*-chlorobenzaldehyde and *p*-nitrobenzaldehyde condensed as easily as the *o*-nitro-derivative with diethylaniline to form similar products.

18. Perchloroformic Ether.—Hentschel (Ber. **18**, 1,177) has made a full investigation of the condensing powers of perchloroformic ether. The preparation of the ether itself is described by him as follows. A flask containing liquid phosgene is placed in a freezing mixture and connected with a reflux condenser. Methyl alcohol is then added slowly. Each drop of the alcohol dissolves with a hissing sound, and torrents of methyl chloride are evolved. As soon as the addition of alcohol calls forth no further action the ester is poured into water, washed, and dried with calcium chloride.

This methyl ester of chloroformic acid boils at 69-71°. When it is submitted to the action of chlorine in sunlight (J. pr. Ch. **144**, 100), perchloroformic ether is obtained.

This substance has a very considerable condensing power. Thus when it is added to a mixture of dimethylaniline and benzaldehyde a few minutes' warming on the water bath converts the whole into the leuco base of malachite-green.

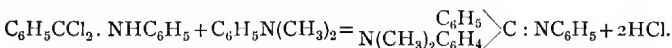
The use of this substance on a large scale is frequent, but in such cases it is generally mixed with aluminium chloride.

19. Phosgene.—This substance seems to be used in manufacturing (Ger. Pat. 62,539) as a condensing agent.

20. Phosphorus Oxychloride.—Nencki (M. f. Ch. **9**, 1,148) prepared the leuco base of malachite-green by warming benzaldehyde (40 gr.) and dimethylaniline (100 gr.) with 93 per cent. alcohol (40 grs.) in a flask of two litres capacity attached to a reflux condenser. Through a small separating funnel he allowed phosphorus oxychloride (65 gr.) to flow slowly into the warm liquid. When the whole had been added the heating was continued for half an hour, and then the liquid was dissolved in water, and the solution filtered. On adding the proper amount of caustic soda the leuco base was precipitated as an easily crystallisable oil, and in almost quantitative amount.

For use on a large scale the following method is prescribed. Benzanilide (20 parts) and dimethylaniline (40 parts) are mixed with phosphorus oxychloride (20 parts), and the whole gently warmed on the water bath and constantly stirred. As soon as a marked rise in the temperature sets in, due to development of heat by the action, the vessel is removed from the water bath, and the progress of the action regulated by cooling, so that the temperature does not exceed 120°. When the action becomes less energetic the heating on the water bath is renewed for one or two hours. The syrupy mass which remains contains the condensation product.

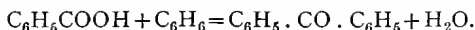
According to Friedländer's "Farbenfabrikation" (p. 47), dichlorobenzyl-anilide is first formed, and this interacts with the tertiary amine, producing a substitution derivative of phenylimidobenzophenone—



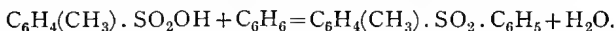
This agent can also be used for internal condensation (Ber. **20** 2,863).

21. Phosphorus Pentoxide.—This substance is an excellent condensing agent, as might be expected from its powerful attraction

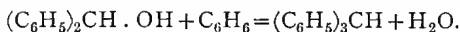
for water. Thus a mixture of benzoic acid and benzene (Kollarits and Merz, Ber. **6**, 537), with phosphorus pentoxide gives diphenylketone—



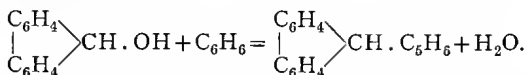
Michael and Adair (Ber. **11**, 116), find that sulphonic acids act similarly. For example, when *p*-toluenesulphonic acid and benzene are heated with the pentoxide in a sealed tube at 150–170°, a certain amount of phenyltoluylsulphone is produced—



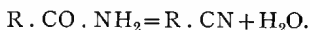
According to Hemilian (Ber. **7**, 1,204), when the pentoxide is covered with a solution of benzhydrol in pure benzene in a sealed tube and heated for four hours, 50 per cent. of the possible quantity of triphenylmethane can be obtained by washing away the phosphoric acid with water and distilling—



By using fluorenyl alcohol (Ber. **11**, 202), he prepared diphenylenephénylmethane—

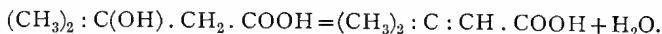


The pentoxide can also be used in intramolecular condensation as in the formation of nitriles from amides—



Knorr (Ber. **17** 2,863) obtained dimethylfurfurane dicarboxylic ether (carbopyrotartaric ether) by the action of a concentrated solution of phosphoric acid on diacetosuccinic ether.

22. Phosphorus Trichloride.—The use of phosphorus trichloride in the intramolecular extraction of water was first noticed by Frankland and Duppa (Ann. **136**, 16). An early example of its application in this way is given by Semljanitzin and Saytzeff (Ann. **197**, 73). They placed the trichloride (2 mol.) in a retort and added gradually β -oxyisovaleric ether (3 mol.) and heated the mixture in the water bath until the evolution of hydrochloric acid ceased. On adding water, dimethylacrylic ether separated as an oily layer—



This agent is used also on a manufacturing scale. For example, finely pulverised dry tetramethyldiamidobenzophenone (10 parts)

is dissolved in hot dimethylaniline (20 parts), and, when the solution is cold, the trichloride (6 parts) is added. The interaction begins at once, and the mixture becomes blue in colour and mobile. After a short time crystallisation begins, accompanied by much evolution of heat. The temperature is controlled by cooling, and the mass soon becomes entirely solid. After remaining for a few hours the product is dissolved in warm water, and, after the addition of a slight excess of caustic soda, the excess of dimethylaniline is driven off with steam.

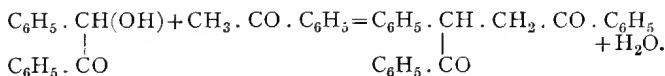
23. Potassium Bisulphate.—Wallach and Wüsten (Ber. 16, 149) made a special study of the applicability of this substance as a condensing agent, and they found it of considerable value. Thus when benzaldehyde (2 parts), dimethylaniline (5 parts), and potassium bisulphate (6 parts) are heated in a flask, immersed in a paraffin bath, to 120–150° for four to six hours, the leuco base of malachite-green is formed, and can easily be extracted from the product in a pure form. Nitrobenzaldehyde acts as easily as benzaldehyde itself.

Experimenting in another direction, they obtained the monomethyl ether of resorcinol by heating resorcinol (1 mol.), methyl alcohol (1 mol.), and bisulphate (1 mol.), for ten hours at 180°.

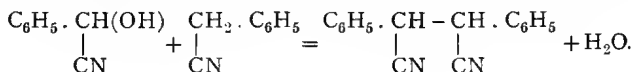
On a large scale it can be used with advantage for the condensation of aldehydes with secondary and tertiary amines and phenols, and of alcohols with phenols. For example, benzaldehyde (21 parts), naphthol (58 parts), and potassium bisulphate (54 parts), are heated for some hours at 150°. The mass is dissolved in alkali and the excess of benzaldehyde expelled with steam, and the condensation product is finally precipitated by addition of an acid. In this, as in many other cases, sodium and ammonium bisulphates may be used in place of the potassium salt.

It may be well here to mention also the use of the bisulphate in distilling glyceric acid and tartaric acid (Erlenmeyer, Ber. **14**, 321) to obtain pyruvic acid. The latter yields 50-60 per cent. of the theoretically possible amount.

24. Potassium Cyanide.—It has been shown by A. Smith (J. Ch. Soc. **57**, 643; Ber. **26**, 60) that benzoin and other ketols condense with acetophenone when boiled with this ketone in dilute alcoholic solution in presence of a small quantity of potassium cyanide. Benzoin yields desylacetophenone.



Knoevenagel (Ber. **25**, 294) finds that the nitrile of mandelic acid and benzyl cyanide condense in presence of dilute potassium cyanide solution to form the nitrile of diphenylsuccinic acid—



25. Potassium Hydroxide.—Heintz (Ann. **169**, 117) was probably the first to examine carefully the condensing power of caustic potash. He found that pure acetone was not influenced by it, but that impure acetone gave “polyacetone.”

Japp and Streatfield (Ber. **16**, 276) found that this hydroxide was a much more convenient agent than ammonia for preparing phenanthroxyleneacetoacetic ether. They mixed pulverised phenanthrenequinone (100 gr.) with acetoacetic ether (90 gr.), added 16 per cent. caustic potash solution (150 cc.), and warmed the mixture gently. The temperature rose markedly, and the colour of the solution changed as the action progressed. The yield was very good.

Fossek (M. f. Ch. **4**, 664) prepared di-isopropylglycol from isobutyric aldehyde by the action of alcoholic caustic potash.

As in the case of ammonia, very small amounts of caustic potash seem to suffice to induce condensation.

For example, Vogtheer (Ber. **25**, 635) found that on mixing equi-molecular proportions of amidodimethylaniline and benzil in alcoholic solution no action took place. But as soon as a few drops of caustic potash were added an almost quantitative yield of red crystals was deposited. The substance had the formula $\text{C}_{22}\text{H}_{20}\text{N}_2\text{O}$, and was formed by loss of one molecule of water.

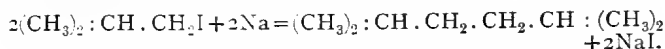
26. Silicic Ether.—Ladenburg (Ann. **217**, 78) experimented with silicic ether as a condensing agent to convert the tropic acid salt of tropine into atropine.

27. Silver.—In the finely divided state silver has the power of removing halogen atoms from organic compounds and so permitting the union of the residues.

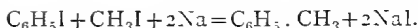
28. Sodium.—In many condensations sodium is preferable even to that marvellously useful substance sodium ethylate.

Wurtz (Ann. **96**, 365) was the first to employ sodium for con-

densation by preparing di-isobutyl by the action of the metal on isobutyl iodide—

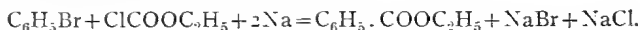


Potassium acts too violently, and cannot therefore take the place of sodium. This reaction acquired more prominence when Fittig (Ann. **149**, 342) found that different radicals could be linked together by its means. For example, he built up homologues of benzene—

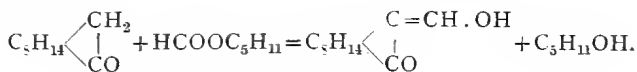


The usual course of the method is to dilute the iodides with dry ether, benzene, or toluene, and add about one and a half times the calculated amount of the metal in thin clean slices. The vessel is connected with a condenser, and is also cooled during the addition of the sodium. As warming often causes the action to proceed with extreme violence, it is better to allow it to go on slowly in the cold. The yields reach 50–75 per cent. of the theoretical.

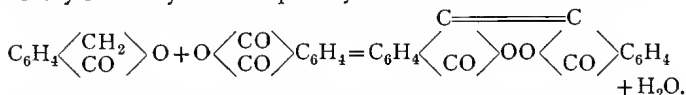
Sodium amalgam was used by Wurtz (Ann. Suppl. **7**, 125), particularly in the preparation of carboxylic acids. For example, he heated bromobenzene (90 gr.) with chlorocarbonic ether (60 gr.) and one per cent. sodium amalgam (3·5 kilos.) for several days in a brine bath at 110° , using a reflux condenser. At the expiration of this time he poured the mercury away from the solid mass of salt, extracted the latter with ether, and obtained benzoic ether by fractional distillation of the extract—



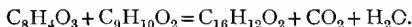
Oxymethylenecamphor (Ann. **281**, 331) is prepared by Bishop, Claisen, and Sinclair as follows: Sodium (1 mol.) in form of wire is placed in a large flask containing dry ether. Camphor (1 mol.) dissolved in ether, and finally amyl formate in slight excess are added in small portions at a time. The materials are carefully cooled during the entire operation. After the mixture has remained for a considerable time, ice-cold water is added, the ethereal layer is removed, and the substance precipitated from its alkaline solution by means of acetic acid. The substance, at first oily, soon becomes crystalline—



29. Sodium Acetate.—This substance is used as a condensing agent in the anhydrous form, and is prepared for the purpose by fusing the ordinary crystalline sodium acetate. For example, Gräbe and Guye (Ann. **233**, 241) heated a mixture of phthalide (10 parts) and phthalic anhydride (17–20 parts) with the acetate (5 parts) for ten hours at 260–265°. On extracting the resulting mass with water and a small quantity of alcohol, a fifty-five per cent. yield of crystalline diphtalyl remained—



Ruhemann (Ber. **24**, 3,965) fused paratoluylacetic acid (1 part) with phthalic anhydride (1½ parts) and sodium acetate ($\frac{1}{10}$ part) in a small flask. The progress of the action could be traced by the rate of evolution of carbon dioxide and steam. The product was *p*-xylidenephthalide, and the yield was 75 per cent. of the theoretical—



Gabriel (Ber. **17**, 1,389) made some experiments on the condensation of phthalic anhydride with acetoacetic ether in presence of sodium acetate, and found that very complicated derivatives were formed.

A thorough examination of the subject by Liebens (M. f. Ch. **1**, 818), has shown that even solutions of sodium acetate in water have some condensing power.

30. Sodium Ethylate.—The use of this remarkable condensing agent is due to Claisen (Ber. **20**, 655).

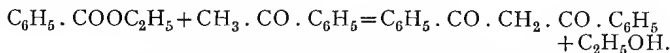
When solid sodium ethylate is used it should be freshly prepared, ground in a warm iron mortar, and rapidly passed through a fine sieve; it cannot be preserved, except in hermetically sealed glass flasks, as it absorbs not only moisture, but also oxygen. Hemmelmayr (M. f. Ch. **12**, 115) has shown that it is converted into sodium acetate.

When more than a very small quantity of sodium ethylate, free from alcohol, is required, it cannot easily be prepared in glass vessels, as they are liable to crack. Claisen uses a copper cylinder, the head of which is fastened on with clamps, and heats it in an oil bath at 200°. The sodium is dissolved in portions in absolute alcohol in a large flask attached to a reflux condenser, and the saturated solution is poured through a tube in the lid into the cylinder. The alcohol distils off through another tube connected

with a condenser, and can be used again with fresh absolute alcohol for dissolving more sodium. A slow stream of dry hydrogen passes constantly through the apparatus, entering by the first tube, and serves to prevent access of air and to sweep out the last traces of alcohol vapour; by this process several kilograms of the substance can be prepared in a day.

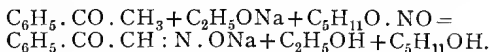
Small quantities can be made by a method suggested by Brühl and Biltz (Ber. **24**, 649). The methyl or ethyl alcohol is dissolved in benzene or xylene, and the theoretical amount of sodium is added. The mixture has to be heated in a flask attached to a condenser for a considerable time, because the alcoholate is insoluble in the hydrocarbon and tends to protect the metal from further action; shaking the vessel helps to break the crusts of alcoholate. Finally, the product remains as a white gelatinous substance suspended in the diluent.

Many condensations have been carried out by Claisen with this agent. For example, dibenzoylmethane (Ber. **20**, 655) was formed from benzoic ether and acetophenone, and the action is a general one for esters and ketones—



He mixed the pulverised sodium ethylate with molecular quantities of the other ingredients, and found that the liquid mixture soon became warm and solidified to a mass consisting chiefly of the sodium salt of dibenzoylmethane; the product is dissolved in water and the diketone precipitated by means of a stream of carbon dioxide; the amount of the substance obtained is equal to fifty per cent. of the acetophenone used.

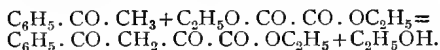
By the help of the same condensing agent he also prepared nitroso-ketones from mixtures of ketones with nitrous ether; in such cases the ethylate did not require to be free from alcohol. Thus sodium was dissolved in twenty times its weight of alcohol, the solution was cooled, and acetophenone and amyl nitrite added. After the liquid had remained at a low temperature for twelve to twenty-four hours the reddish-brown sodium salt of the nitroso-ketone crystallised out—



On adding an acid the nitroso-ketone was obtained in the free state.

Benzoylacetone (Ber. **20**, 2,178), $C_6H_5.CO.CH_2.CO.CH_3$, is prepared by covering dry sodium ethylate (1 mol.) with excess of acetic ether (2 mol.), cooling the mixture in ice and adding acetophenone (1 mol.). The mass first becomes fluid and then solid again, owing to the separation of the sodium salt of benzoylacetone. The yield is equal to 80-90 per cent. of the acetophenone taken. The higher homologues are formed by taking the corresponding esters.

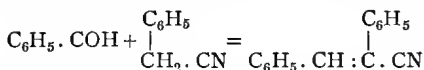
Benzoylpyruvic acid is prepared by dissolving sodium (9.2 gr.) in alcohol (150 gr.), cooling the solution in ice, adding acetophenone (48 gr.) and oxalic ether (58.4 gr.) and shaking the mixture. After the liquid has remained for twelve hours a large amount of the sodium salt is deposited. The yield is 78 per cent. of the theoretical—



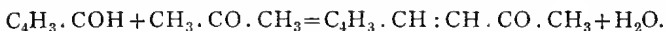
Benzoylaldehyde, $C_6H_5.CO.CH_2.CO.H$, whose preparation in other ways had been attempted in vain, was made by Claisen by dissolving sodium (1 atom) in twenty times its weight of alcohol, cooling in ice, and adding acetophenone (1 mol.) and formic ether (1 mol.). The sodium salt separated in the course of two or three days, and the yield was good.

The method has been found to be applicable on a large scale, and is used for the preparation of diketones and of esters of keto-acids.

An application made by V. Meyer (Ann. **250**, 124) may be mentioned. He treated benzyliocyanide and benzaldehyde with sodium ethylate. The mixture became warm and gave a solid mass of benzyliidenebenzyliocyanide, the nitrile of α -phenylcinnamic acid—



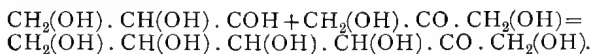
31. Sodium Hydroxide.—The condensing power of very dilute caustic soda was first noticed by Schmidt (Ber. **14**, 1,459), and has been carefully investigated by Claisen (Ber. **14**, 2,468). Many interactions proceed in presence of caustic soda with extreme ease; as, for example, the union of furfural and acetone to form furfurylideneacetone—



According to Geigy and Königs (Ber. **18**, 2,406), quantitative yields can be obtained by choosing the proper strength of the alkaline solution; in some cases boiling must be resorted to.

Fischer (Ber. **20**, 3,386) oxidised glycerol with bromine and carbonate of soda, obtaining a solution which contained glyceric aldehyde, and also the isomeric dioxyacetone. By adding this

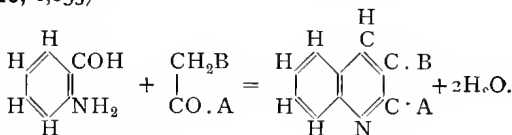
solution to a liquid containing one per cent. of caustic soda, and allowing the mixture to remain for four or five days at 0° , he obtained a sugar,¹ α -acrose.



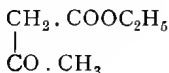
Einhorn and Diehl (Ber. **18**, 2,320) allowed 10 per cent. caustic soda to drop into a mixture of cinnamic aldehyde (10 parts) and acetone (6 parts). At first the alkaline reaction disappeared and the liquid became warm. It was cooled with water, and the addition of the alkali continued until the alkaline reaction became permanent. After the lapse of twelve hours the mixture was poured into water. The oil which separated soon solidified. It was composed of two substances which could be separated by repeated recrystallisation from absolute alcohol. There were formed cinnamylvinyl methyl ketone and dicinnamylvinyl ketone.

Einhorn and Gehrenbeck (Ann. **253**, 353) dissolved *p*-nitrobenzaldehyde (5 gr.) in boiling absolute alcohol (80 gr.), added water (15 cc.), and allowed the solution to cool until it began to show turbidity. They then added acetone (10 gr.), and finally 2 per cent. caustic soda drop by drop until the alkaline reaction remained for five minutes. In this way they obtained compounds corresponding to those described above.

Friedländer (Ber. **15**, 2,574) prepared quinoline by adding a few drops of caustic soda to a solution of *o*-amidobenzaldehyde and acetic aldehyde in dilute water solution, and then setting the base free by addition of excess of alkali. He found that this method was of almost perfectly general applicability for obtaining quinoline derivatives having various groups attached to the pyridine nucleus (Ber. **16**, 1,833)—



For example, acetoacetic ether—



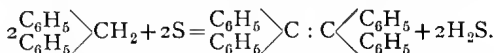
can take the place of the aldehyde, and when it is used crystals of

¹ The syntheses of sugars are treated fully in the author's "Moderne Chemie, zwölf Vorträge vor Aerzten gehalten." Hamburg, 1891.

α -methylquinoline β -carboxylic ether are almost immediately deposited.

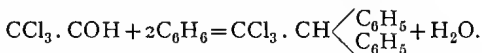
Victor Meyer (Ber. **17**, 1,078), having found that sodium ethylate gave a very bad yield, condensed methyl iodide and benzyl cyanide by means of solid caustic soda. He used freshly-fused and pulverised sodium hydroxide (1 mol.), added molecular proportions of the other ingredients, and warmed the mixture. The interaction took place with violence, and was completed by gently heating in the water bath. The product contained methylbenzyl cyanide along with some unchanged benzyl cyanide.

32. Sulphur.—This substance has the power of removing hydrogen and so inducing condensation. Thus Ziegler (Ber. **21**, 780) prepared tetraphenylethylene by heating diphenylmethane (20 gr.) with sulphur (8 gr.) in an oil bath at 240–250°—

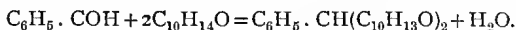


The union of dissimilar radicals by this means does not seem to have been investigated.

33. Sulphuric Acid.—The condensing power of sulphuric acid depends on its very strong attraction for water. Thus Baeyer (Ber. **5**, 1,098) mixed benzene (2 mol.) with chloral (1 mol.) and added an equal volume of concentrated sulphuric acid. On shaking the mass became warm, and external cooling was used to keep the temperature down. The upper blue-coloured layer was poured off and shaken with fresh acid until it turned into a crystalline mass. This was washed with water and purified by recrystallisation. The yield of trichlorodiphenylethane was quantitative—



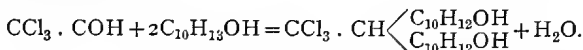
Similarly benzaldehyde (1 mol.) was mixed with thymol (2 mol.) and slightly diluted (4 : 1) sulphuric acid (10 cc.). The acid was added drop by drop, with an interval after the addition of the first half to allow the mixture to cool. On shaking, the mass crystallised and dithymolphénylmethane was formed. The yield was about 85 per cent. of the theoretical—



Böttger (Ber. **14**, 1,595) prepared diphenylpropionic acid by allowing pyruvic acid to flow into ten times its volume of concentrated sulphuric acid cooled to -10° . On adding benzene and shaking, the latter froze in contact with the cold acid. The flask was then removed from the freezing

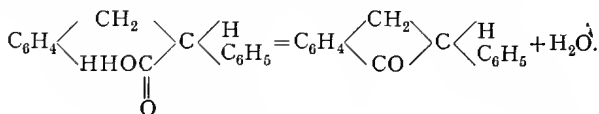
mixture and the shaking continued. The temperature gradually rose, and the action was complete before the thermometer registered $+10^{\circ}$. Above this temperature decomposition takes place.

A modification of this plan was introduced by Jäger (Ber. **7**, 1,197). He dissolved thymol (2 mol.) in chloral (1 mol.) and added four or five times its bulk of sulphuric acid diluted with one third of its volume of glacial acetic acid. The trichlorodithymolethane was gradually deposited as a soft mass which became granular on addition of water—



This use of sulphuric acid and acetic acid together seems to be advantageous in many cases. Thus Königs (Ber. **24**, 180) mixed dihydronaphthalene (40 gr.) and phenol (28 gr.), cooled the mixture, added pure sulphuric acid (40 cc.) and glacial acetic acid (40 cc.), and shook the whole at intervals during twenty-four hours. Under these circumstances the product became acetylated, and this part of the action had to be undone by boiling the product with alcoholic caustic potash. Tetrahydronaphthylphenol, $\text{C}_{10}\text{H}_{11} \cdot \text{C}_6\text{H}_4 \cdot \text{OH}$, is formed by addition, the yield being seventy per cent., but its purification is far from simple.

Sulphuric acid is likewise applicable in cases of internal condensation. Thus Miller and Rohde (Ber. **25**, 2,095) obtained phenylhydrindone from α -phenylhydrocinnamic acid—

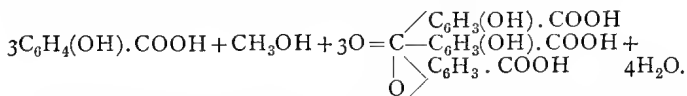


They added the dry pulverised acid (10 gr.) to concentrated sulphuric acid (80 gr.) at a temperature of 140° . The mixture was shaken till solution was complete, an operation which occupied only a few seconds, and then the brown effervescing mass was poured at once upon three times its weight of ice. The resulting milky liquid deposited gradually a flocculent crystalline precipitate of phenylhydrindone.

For such internal condensations phosphoric acid (Ann. **234**, 241) or fuming sulphuric acid is frequently added.

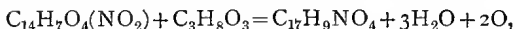
A combination of condensation and oxidation is used in the preparation of aurin tricarboxylic acid (Ber. **25**, 939). This substance

is formed by the action of salicylic acid (3 mol.) on methyl alcohol (1 mol.), for which formaldehyde or methylal can be substituted, in presence of sulphuric acid and sodium nitrite—

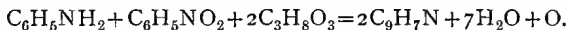


There may be a difference of opinion as to whether Skraup's synthesis of quinoline can be regarded as a case of oxidation combined with condensation or not, but the method demands a place here on account of its importance.

In 1877 Prudhomme (Ber. **11**, 522) stated that nitroalizarin gave a blue colouring matter when heated with glycerol and sulphuric acid. Following this up Brunk devised a method of preparing the substance on a large scale by the action of glycerol and sulphuric acid on alizarin and nitroalizarin at a high temperature. A little later Gräbe (Ber. **11**, 1,646) expressed the opinion that the glycerol not only acted as a reducing agent, but also took part in a remarkable synthesis expressed by the equation—



producing a substance, $\text{C}_{17}\text{H}_9\text{NO}_4$, which was closely related to quinoline. Finally this led Skraup (M. f. Ch. **2**, 141) to investigate the action of sulphuric acid on glycerol and nitrobenzene. He added also aniline in order to supply the oxygen set free by the action with a substance which it could easily oxidise. Quinoline was formed in accordance with the equation—

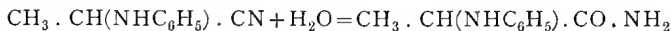


In practice nitrobenzene (144 parts), aniline (216 parts), glycerol of sp. gr. 1.24 (600 parts), and sulphuric acid (600 parts), are mixed together (Am. Pat. 241,738) in a flask connected with a reflux condenser and heated, at first gently and later more strongly, for several hours. The mixture is then diluted with water, and the unchanged nitrobenzene driven over with steam. On now adding caustic soda the quinoline is set free and can likewise be driven over. The yield is about seventy per cent. of the theoretical.

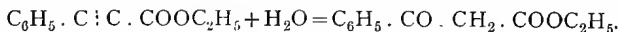
A great variety of quinoline derivatives can be prepared by this method, by using, instead of aniline and nitrobenzene, their homologues and isologues. Whether these can be replaced by substances resembling them in chemical properties while differing from

them in chemical nature (isidioms, Ber. **25**, 2,394) does not seem to have been investigated.

In connection with this subject mention must be made of the interesting cases in which concentrated sulphuric acid brings about the *addition of water*. The acid has the power, for example, of transforming nitriles into amides. Thus Tiemann and Stephan (Ber. **15**, 2,035) mixed α -anilidopropionitrile with sulphuric acid guarding at the same time against any considerable rise in temperature in the mass. After the mixture had remained at rest for a sufficient time, addition of water precipitated none of the unchanged nitrile, and on adding ammonia to the diluted solution the amide was thrown down—



Baeyer (Ber. **15**, 2,705) dissolved phenylpropionic ether in sulphuric acid, allowed the solution to remain for some time, and then poured it on to ice. By purifying the oil which separated benzoylacetic ether was obtained—



He found that phenylacetylene, amidophenylacetylene, and *p*-nitrophenylpropionic acid had the same property.

Flawitzki and Krylow (Centralblatt, **1878**, 262) found that methylisopropylketone, $(\text{CH}_3)_2 : \text{CH} \cdot \text{CO} \cdot \text{CH}_3$, was formed when isopropylacetylene, $(\text{CH}_3)_2 : \text{CH} \cdot \text{C} : \text{CH}$, was shaken with sulphuric acid sp. gr. 1.64.

The student may be reminded in conclusion of the use of a few drops of sulphuric acid in converting polymerised aldehydes into the simple forms. Thus Weidenbusch (Ann. **66**, 157) converted paraldehyde into aldehyde, and Fosseck (M. f. Ch. **4**, 662) tri-isobutyric aldehyde into isobutyric aldehyde by this means.

34. Tin Tetrachloride.—Baeyer (Ann. **202**, 68) found in this substance the most efficient condensing agent for preparing phthaleins. He heated phthalic anhydride with phenol and stannic chloride for five hours at 120° . The resulting reddish-brown mass was warmed with water on the water bath and the residue dissolved in sodium carbonate. The solution was filtered from the precipitate, which contained the tin. The phthalein was deposited in an almost pure condition on the addition of hydrochloric acid to the filtrate.

Graebe (Ann. **247**, 286) heated diphenyleneketone carboxylic

acid (15 gr.) with phenol (20 gr.) and stannic chloride (25 gr.), obtaining an excellent yield (20–22 gr.) of the condensation product.

Fabinyi (Ber. **11**, 283) added the chloride drop by drop to a cold mixture of phenol and paraldehyde until, even after the lapse of half an hour, the fumes of stannic chloride were still perceptible. After washing the product with water and distilling it *in vacuo*, he obtained diphenolethane—

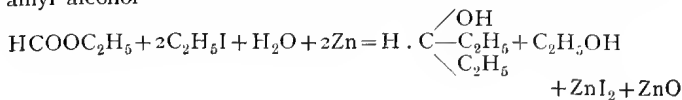


Steiner (Ber. **11**, 286) recommends the dilution of the chloride with chloroform.

Michael (Ber. **16**, 2,298) heated phenol (50 gr.) and salicylic acid (50 gr.) with stannic chloride (40 gr.) for fourteen hours at 115–120°, raising the temperature finally to 125°. The phenol was removed with steam, and the residue boiled with great excess of sodium carbonate. Carbon dioxide precipitated salicylphenol, $\text{CO} \begin{smallmatrix} \diagup \text{C}_6\text{H}_4\text{OH} \\ \diagdown \text{C}_6\text{H}_4\text{OH} \end{smallmatrix}$, from the filtrate. The yield was much better than when zinc chloride was used.

35. Zinc.—This substance was first used as a condensing agent by Frankland and Duppa (Ann. **133**, 80). They began by causing zinc ethyl to act upon oxalic acid, but found later that the same end was attained by the action of zinc on ethyl iodide and oxalic ether. Thus they mixed methyl iodide (2 mol.) with methyl oxalate (1 mol.) and excess of amalgamated granulated zinc, and heated the whole in a flask attached to a condenser, the top of which was connected with a tube dipping into mercury. Methyl dimethyloxyacetate was produced as the result of continuous heating for twenty-four hours, at first at 70° and later at 100°. Later investigations showed that it was preferable (Ann. **135**, 25) to allow the mixture to stand for four days without heating.

This method is susceptible of general application. For example, Saytseff (Ann. **175**, 363) mixed formic ether (1 mol.) with an excess of ethyl iodide (4 mol.), and added some zinc-sodium and so much dry finely granulated zinc that it was not completely covered by the liquid. After heating the whole, with a reflux condenser attached, and decomposing the product with water, he obtained secondary amyl alcohol—



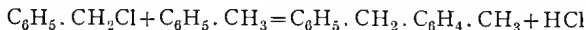
In these cases, therefore, the carbonyl oxygen was replaced by two alkyl groups.

Hofmann (Ann. **201**, 85) has shown that allyl iodide can be used in the same way as the saturated alkyl iodides.

The amalgamated zinc mentioned above was used also by Daimler (Ann. **249**, 174). He prepared it by dipping the granulated metal into a dilute solution of mercuric chloride, and washing and drying it.

In preparing naphthyl ketones from naphthalene and benzoyl chloride, Kegel (Ann. **247**, 1,807) mixed the ingredients, using one and a half molecular proportions of the naphthalene, and, to avoid over violent action, merely dipped a small strip of zinc into the heated liquid. Two ketones were formed.

Zincke (Ann. **159**, 373) boiled benzyl chloride (100 gr.) and toluene (72 gr.) with zinc, and obtained 32 grams of distillate and 90 grams of residue. The interaction took place in accordance with the equation—



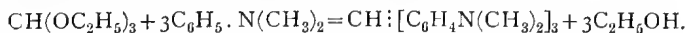
36. Zinc Chloride.—The use of this substance was first discovered by O. Fischer (Ann. **206**, 86), who drew attention to the fact that it had a surprisingly great condensing power, even approaching aluminium chloride itself in this respect. He used the chloride in the form of a fine powder, and pointed out that, to give good results, it should be pure. In particular, it should be free from the basic carbonate which the commercial chloride often contains. In making fused zinc chloride, copper basins are said to be the best vessels to use. Merz and Müller (Ber. **19**, 2,902) state that it can be obtained by passing excess of hydrochloric acid gas into the common chloride which has been fused in a retort. Usually no great amount of the gas is required. The excess is expelled with dry hydrogen.

The following preparation illustrates Fischer's method. Dry chloride of zinc is added, a little at a time, to a mixture of phthalic anhydride (1 mol.) and dimethylaniline (2 mol.) until an amount of it equal to that of the base has been used. The action begins at 100°, and the mixture is warmed and stirred on the water bath for several hours. To complete the action it is heated for four hours in an oil bath at 120–150°. The mixture becomes gradually semi-solid, and on cooling forms a hard, brittle lump. This is dissolved in dilute hydrochloric or sulphuric acid, and the solution is placed

in a large flask along with excess of concentrated caustic soda. The unused dimethylaniline is driven off with steam, and the phthalein solidifies on cooling in the residue. The yield is about 50 per cent. of the theoretical—



Fischer and Körner (Ber. **17**, 99) heated orthoformic ether (1 part) with dimethylaniline (3-4 parts) on the water bath for several hours, and added the chloride (2 parts) gradually. The hexamethylparaleucaniline which was formed was isolated from the resulting blue mass by driving off the excess of dimethylaniline with steam, dissolving the residue in hydrochloric acid and pouring the solution into cooled ammonia. The base was deposited in crystalline form and almost theoretical amount—



When substances prepared by this method are soluble in water they are extracted with ether.

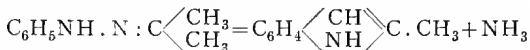
Zinc chloride has also the power of condensing acid chlorides with anhydrides. Thus Doebner (Ber. **14**, 648) heated benzoic anhydride with benzoyl chloride in a flask provided with a condensing tube. The action was started and maintained by adding small amounts of zinc chloride from time to time. At the end of eight hours fresh additions of the chloride produced no further evolution of hydrochloric acid. The product was benzoylbenzoic acid, $\text{C}_6\text{H}_5 \cdot \text{CO} \cdot \text{C}_6\text{H}_4 \cdot \text{COOH}$.

Liebmann (Ber. **14**, 1,842) dissolved phenol (100 gr.) in isobutyl alcohol (80 gr.), and heated it with zinc chloride (240 gr.) in a flask attached to a condenser. One molecule of water was eliminated, and as soon as the evolution of white vapours began, an indication that decomposition was taking place, he allowed the mass to cool, and dissolved it in water acidulated with hydrochloric acid. On distilling the supernatant oil he obtained isobutylphenol (105 gr.) $\text{C}_4\text{H}_9 \cdot \text{C}_6\text{H}_4 \cdot \text{OH}$.

Hantzsch (Ber. **13**, 1,347) states that when naphthylamine (3 parts) is heated in a sealed tube with an equal amount of methyl alcohol and zinc chloride (4 parts) at $180-200^\circ$, ammonia is evolved and an almost quantitative yield of α -methoxynaphthalene obtained.

This power which zinc chloride has of effecting syntheses with elimination of ammonia was used by E. Fischer (Ann. **236**, 116) for the synthesis of indole derivatives. He found that phenylhydrazones of aldehydes and ketones were easily converted into

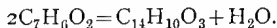
indoles by loss of ammonia. Thus, when acetone phenylhydrazone is heated to 170–180° with four or five times its weight of zinc chloride, the action begins almost immediately, and when it is over a molten dark-coloured mass remains. This is treated with water and the α -methylindole driven over with steam. It appears as an almost colourless oil which soon solidifies in the receiver. The yield is more than sixty per cent. of the theoretical—



Chloride of zinc can also be used for the synthesis of pyrrole derivatives (Ber. **20**, 851), but the yields attained so far have been rather poor.

It has already been pointed out (Chap. II. § 4), that zinc chloride assists greatly the introduction of acetyl groups by means of acetic anhydride. When glycerol is mixed with four times its weight of acetic anhydride and a little piece of the chloride is added, the action is explosively violent (Ber. **12**, 2,059). Erwig and Königs (Ber. **22**, 1,465) obtained the pentacetyl derivative of grape sugar by dissolving a little zinc chloride in 20 cc. of acetic anhydride and adding 5 grams of dextrose to the boiling-hot solution. The yield was sixty per cent. When the action took place at 100° and the solution was boiled for a short time, after remaining on the water bath for half an hour, octacetyldiglucoose was formed.

Zinc chloride has some condensing power in solution, although in most cases the yields are better when the substances are fused together without a solvent. Thus Bourquin (Ber. **17**, 502) dissolved zinc chloride (3 parts) in warm glacial acetic acid (2 parts), added salicylic aldehyde (1 part), and heated the whole for a short time at 145°. The condensation product was separated by pouring the solution into water—



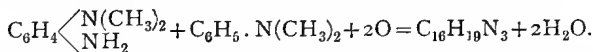
If the acetic acid is removed by distillation, instead of by pouring into water, it is found to have acquired condensing powers which it does not ordinarily possess.

Friedländer and Weinberg (Ber. **15**, 2,103) warmed amidocinnamic ether in a saturated alcoholic solution of zinc chloride at 80–90°. On rendering the solution alkaline they found that ethoxyquinoline was driven over by steam.

The investigations of Varennes (Bull. Ch. **40**, 266) illustrate well the statement made above, that condensing agents are not

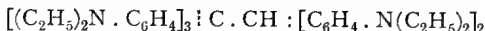
interchangeable. He found, for example, that no mesitylene was formed from acetone by the action of zinc chloride. But when acetone (180 gr.) and sulphuric acid (300 gr.) were warmed for an hour, and steam finally driven through the mixture, 40 grams of impure mesitylene were carried over.

A combination of condensation and oxidation was used by Bindschedler (Ber. **16**, 865). He took an aqueous solution of dimethyl-*p*-phenylenediamine (1 mol.) and dimethylaniline (1 mol.) containing a little zinc chloride, and treated it, at 30°, with as much potassium bichromate as would release two atomic proportions of oxygen. In a few minutes glittering copper-coloured crystals of pure "dimethylphenylene green" were deposited—



The temperature used in zinc chloride condensations may have an important influence on the result. Where nitro-derivatives are used it is especially necessary to keep the temperature as low as possible. Thus Fischer and Schmidt (Ber. **17**, 1,889) found that in condensing *o*-nitrobenzaldehyde (1 part) with dimethylaniline (3-4 parts), the mixture had to be warmed on the water bath, the zinc chloride (1 part) added very slowly, and the greatest care taken to keep the temperature from exceeding 100°. When sufficient care was not taken the mass became resinised through the oxidising influence of the nitro-group. On the other hand with careful treatment an almost quantitative yield was attained.

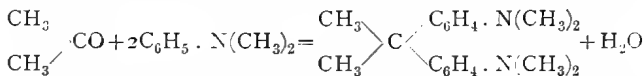
The different effects of different temperatures may be further illustrated by reference to some experiments described by Boessnek (Ber. **19**, 367). When chloral hydrate (20 parts), diethylaniline (50 parts), and zinc chloride (10 parts) are allowed to interact at 100° the mixture becomes green in colour and stiff in consistency at the end of five hours. If the mass is now dissolved in dilute sulphuric acid a substance having the constitution



is precipitated. When, instead of heating the substances, zinc chloride (10 gr.) is mixed with the chloral hydrate (20 gr.) and diethylaniline (60 gr.) in the cold and the mixture is allowed to remain at 40° for two days, and the mass is dissolved in dilute hydrochloric acid, the addition of ammonia precipitates nothing but zinc hydroxide. This can be dissolved in excess of ammonia,

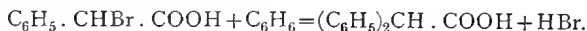
and extraction of the solution with ether then removes a substance having the constitution $\text{CCl}_3 \cdot \text{CH}(\text{OH}) \cdot \text{C}_6\text{H}_4 \cdot \text{N}(\text{C}_2\text{H}_5)_2$.

Doebner (Ber. **12**, 813) heated in a *sealed tube* acetone (1 mol.), dimethylaniline (2 mol.), and zinc chloride (1 mol.) for several hours at 150° . Tetramethyldiamidodiphenyldimethylmethane was formed—



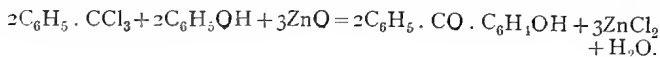
Calm (Ber. **16**, 2,786) found that excellent results could be obtained by using a mixture of zinc chloride and calcium chloride. The yields were sometimes as high as 90 per cent. of the theoretical. Thus he prepared diphenyl-*p*-phenylenediamine by heating quinol (1 mol.) and aniline (4 mol.) with calcium chloride (3-4 mol.) and zinc chloride ($\frac{1}{2}$ mol.) at $200-210^\circ$ in a sealed tube. As good yields as his can now be obtained in open vessels by other methods.

37. Zinc Dust.—Zincke (Ann. **159**, 374) condensed benzyl chloride and benzene to diphenylmethane, $\text{C}_6\text{H}_5 \cdot \text{CH}_2 \cdot \text{C}_6\text{H}_5$, by means of zinc dust. Similarly Symons and Zincke (Ann. **171**, 123) synthesised diphenylacetic acid from phenylbromacetic acid (20 gr.) and benzene (40 gr.). Larger amounts cannot be used at one time as the interaction is very violent. The substances are mixed and warmed on the water bath, and zinc dust is added in small portions as long as hydrogen is evolved from the action of hydrobromic acid on the metal. The action is completed by continuing the heating for several hours—

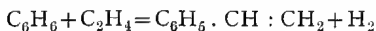


Paal (Ber. **17**, 911) dissolved benzophenone (1 mol.) and acetyl chloride (4 mol.) in dry ether and added zinc dust. The solvent boiled spontaneously, and β -benzpinacolin was formed in quantitative amount. When only one molecular proportion of acetyl chloride was used an equally good yield of α -benzpinacolin was obtained.

38. Zinc Oxide.—Doebner and Stackmann (Ber. **9**, 1,919) acted with benzotrichloride on phenol in presence of zinc oxide and obtained benzoylphenol—



39. Effect of Heat Alone.—We have already seen (Chap. IV. § 8) that when organic bodies are conducted through red-hot tubes all kinds of chemical changes take place. Many of these are of the nature of condensations. Hydrocarbons are particularly liable to lose hydrogen and condense to form larger molecules. Thus benzene and ethylene (Z. Ch. **1866**, 709) form styrene—



CHAPTER XIII

PREPARATION OF DIAZO-BODIES

1. Introductory.—As is well known, Griess was the first to prepare diazo-bodies by the action of nitrous acid on salts of amido-compounds.¹ As they are very powerfully reactive they are frequently prepared, but are less frequently isolated from the solutions in which they are made. The chief reason why they are at once worked up into other compounds is that many of them are highly explosive in the dry condition. For example, diazobenzene nitrate explodes more violently than fulminate of mercury (Berthelot, *Bull. Ch.* **37**, 385) on being slightly warmed.

Diazo-bodies are now seldom prepared by the direct action of free nitrous acid. The usual course is to apply this in the nascent condition by adding sodium or potassium nitrite to an acid solution of the base. In exceptional cases amyl nitrite is employed, and more rarely still silver nitrite or oxidation processes.

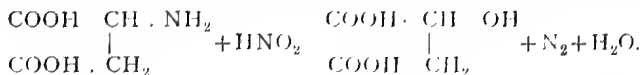
2. Preparation of Nitrous Acid.—The gas is best prepared by warming arsenious oxide with 50 per cent. nitric acid in the water bath. When starch is used in place of arsenious oxide the stream of gas is very rapid, and only lasts a short time. An alternative method is to prepare the gas by the action of dilute sulphuric acid on sodium nitrite.

The exact composition of the gases obtained by such means is uncertain, and doubtless a gas of constant composition is procurable only by working always under the same conditions. Thus

¹ In regard to the direct use of the solutions of amido-compounds obtained by reduction from the corresponding nitro-derivatives, see the chapter on "Reduction" (XIX.) under the use of tin in acid solution.

Silberstein (J. pr. Ch. **135**, 101) found that when nitrous acid, from arsenious oxide and nitric acid, was conducted into tribromaniline, which was partly dissolved and partly suspended in cold water, in a rapid stream, the chief product was tribromodiazobenzene nitrate. When the gas arising from arsenious oxide and nitric acid, without warming, was conducted in a slow stream into the same mixture, hexabromodiazamidobenzene was formed, and much tribromaniline remained unattacked even after prolonged exposure to the action of the gas.

3. Use of Nitrous Acid.—The earliest notice of the interesting action of nitrous acid on amido-derivatives is due to Piria (Ann. **68**, 349). By its action on asparagine in nitric acid solution he obtained malic acid, with intermediate formation of aspartic acid



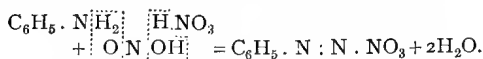
Strecker (Ann. **68**, 54) and others used the same reaction for the production of oxy-compounds.

Ganahl (Ann. **99**, 240) was the first, however, according to Chiozza, to obtain a body containing more nitrogen than the parent substance by the action of nitrous acid on naphthylamine. Griess (Ann. **113**, 207) then obtained, by the action of nitrous acid on a solution of *m*-dinitro-*o*-amidophenol in nitric acid, a substance which he named diazodinitrophenol on account of the fact that it retained the properties of a phenol and had half of its nitrogen bound in a peculiar manner. He soon found (Ann. **120**, 126) that the same action takes place in nitric acid solutions containing alcohol or ether in place of water, that a low temperature is the essential condition for diazotisation, and that the action takes a different course when the amido-body is employed in the free state from that which it follows when the base is combined with an acid.

For example, when nitrous acid acts on amidobenzoic acid in cold alcoholic solution diazoamidobenzoic acid is produced. But if the amidobenzoic acid is dissolved in water or alcohol with nitric acid, the nitrate of diazobenzoic acid is formed, and, if the solution is concentrated, separates as a precipitate.

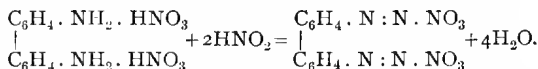
In preparing diazobenzene nitrate he (Ann. **137**, 41) covered aniline

nitrate with a quantity of water insufficient to dissolve it, and, keeping the temperature below 30° , passed nitrous acid into the mixture—



As soon as a sample showed no separation of aniline on addition of caustic potash the reaction was complete, and the solution was filtered and diluted with three times its volume of alcohol. On the further addition of a little ether, the new body came out almost completely in crystalline form.

As early as 1867 (Jahresb. **1866** 461, and J. pr. Ch. **101**, 91), he made the first of the tetrazo-compounds which are now of such importance in the preparation of substantive dyes. He obtained it by treating a solution of benzidine nitrate in water with nitrous acid. On filtering the solution to remove a brown impurity and adding alcohol and ether, tetrazodiphenyl nitrate crystallised out—



Before distilling the mother liquors on the water bath to recover the ether, the liquids must be shaken with water to remove any crystals which may be present in them. Neglect of this precaution may lead to dangerous explosions.

Heinzelmann (Ann. **188**, 174) prepared diazobenzenedisulphonic acid by leading nitrous acid into an alcoholic solution of crystallised aniline-disulphonic acid and precipitating with ether. The product appeared as an oil which solidified on standing over sulphuric acid.

Many diazo-derivatives are insoluble in absolute alcohol. Thus Ascher (Ann. **161**, 8) suspended toluidinesulphonic acid in this solvent, treated it with nitrous acid, and obtained at once diazotoluenesulphonic acid in crystalline form. According to Mohr, however (Ann. **221**, 220), alcohol frequently hinders diazotisation. He found, for example, that *p*-diazobenzylsulphonic acid was not formed on leading nitrous acid into an alcoholic solution of the amido-acid, but that it was formed by covering the acid with water, introducing the nitrous acid, and then precipitating with alcohol.

Many diazo-compounds cannot be removed from solution in water by mixing with alcohol and ether. In such cases they can often be obtained by the addition of mineral acids, sometimes appearing in the form of free diazo-bodies, sometimes in the form of salts.

Thus Kollrepp states (Ann. **234**, 29) that when chloroamido-phenolsulphonic acid was suspended in water, and nitrous acid

conducted into the mixture, a clear solution was soon produced, from which alcohol and ether did not precipitate anything. On now leading gaseous hydrochloric acid into the liquid, crystals appeared, which turned out to be chlorodiazophenolsulphonic acid. They were recrystallised from dilute hydrochloric acid.

Schmitt (Ber. **1**, 67) diazotised amidophenol hydrochloride by covering it with alcohol saturated with nitrous acid and cooling the mixture with ice. Ether was finally added in large quantity, and the solution became nearly solid from the separation of crystalline diazophenol chloride.

4. Use of Sodium Nitrite.—The method of diazotisation by the use of nitrous acid in gaseous form presents many inconveniences, and its use is probably confined to the laboratory. Even there the addition of a solution of sodium nitrite to an acidified solution of the amide is the more usual method (cf. Meyer and Ambühl, Ber. **8**, 1,074). The commercial sodium nitrite contains ninety-eight per cent. of NaNO_2 , and the nitrous acid set free from it acts quantitatively *in statu nascendi*. By this means the operation of diazotisation has been greatly simplified.

Friedländer (Fortschritte d. Farbenfabrikation, I. 542) makes the following clear and precise statement in regard to the process and the behaviour of various bodies when submitted to it:—When the molecular proportion of sodium nitrite dissolved in water is added to acid solutions of aromatic amines, whose salts are soluble in water, such as aniline and xylidine, they are diazotised almost instantaneously. When the salts are difficultly soluble, as with benzdine sulphate, the action may be prolonged through several hours; and the same is true of amidosulphonic acids, such as sulphanilic acid and naphthionic acid, which are usually but slightly soluble. To secure a sufficiently fine state of division, substances of the latter kind are always precipitated from an alkaline solution with acids, and then submitted directly to the action of the molecular proportion of sodium nitrite with previous addition of a corresponding proportion of hydrochloric acid. After the mixture has remained in the cold for several hours the interaction is quantitative as with the former class of bodies.

The following examples illustrate the use of sodium nitrite. Fischer and Kuzel (Ann. **221**, 272) dissolved amidocinnamic acid (10 parts) in a warm mixture of two molecular proportions of hydrochloric acid of sp. gr. 1.19 (9 parts) with water (70 parts).

When the solution cooled crystals separated out in large quantities, and the calculated amount of sodium nitrite was run in, the whole being well cooled and shaken during the process. Usually the crystalline matter passed completely into solution under this treatment, and a little later the chloride of the diazo-compound appeared as a yellow crystalline powder.

Erdmann (Ann. **247**, 329) used a modification of this process in diazotising naphthionic acid. The sodium salt of naphthionic acid (180 gr.) was dissolved in warm water (800 cc.) and the solution allowed to cool. In a large basin 1-2 litres of water were mixed with 13 per cent. hydrochloric acid (650 cc.), or with concentrated sulphuric acid (120 gr.), and the whole was cooled by throwing into it pieces of carefully cleansed ice. Two burettes were suspended over this basin, one filled with 5 per cent. sodium nitrite solution, the other, having a very small exit for the liquid, with the prepared solution of the salt of naphthionic acid. First a few cubic centimetres of the sodium nitrite were allowed to flow into the basin, and then a very small continuous stream of the solution of the organic salt was started. The contents of the basin were violently stirred with a glass rod to prevent the aggregation into lumps of the naphthionic acid which was at first precipitated by the mineral acid. Meanwhile the addition of sodium nitrite was continued at such a speed that the liquid always smelt slightly of nitrous acid, and a piece of filter paper containing starch and potassium iodide was rendered blue by a drop of the mixture. About 760 cc. of the sodium nitrite solution was required.

When the naphthionic acid has all been introduced and the mass has remained at rest for half an hour it must still show the reaction with potassium iodide, as otherwise more sodium nitrite is needed. The yellow diazoamido-compound, after settling, is collected on cheese-cloth, washed with water, pressed to remove the most of the latter, and dried on clay plates *in vacuo* over sulphuric acid. It is better, if the substance is not required in a dry condition, to wash it by decantation, place it in a tall cylinder, and make up the mass to a volume of 1.8 litres. This paste contains 10 per cent. of the diazo-compound which may be preserved for use in this state.

Gabriel (Ber. **15**, 2,295) boiled amidocinnamic acid with 20 per cent. hydrochloric acid (7.5 gr.) and water (27.5 cc.) till the whole went into solution, allowed the liquid to cool, and added to the lukewarm semi-crystalline mass a solution of sodium nitrite (2.5 gr.) in water (50 cc.) in small portions at a time. The mixture became entirely fluid and was rapidly filtered from a small amount of undissolved yellow matter. On adding about twice its volume of concentrated nitric acid yellowish-brown crystals of *o*-diazocinnamic acid (5 gr.) began to collect at the bottom.

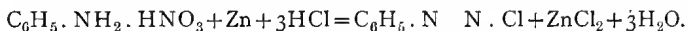
5. Other Ways of Obtaining Diazo-Bodies.—The presence of mineral acids may be avoided by acidifying with oxalic acid instead of hydrochloric or sulphuric acids.

Inorganic substances can be avoided entirely by using amyl nitrite as a source of nitrous acid. Thus Victor Meyer and Ambühl (Ann. **251**, 56) dissolved aniline (2 mol.) in several times its volume of ether, added amyl nitrite (1 mol.), and allowed the mixture to evaporate in open vessels over sulphuric acid. Beautiful golden-yellow transparent crystals of diazoamidobenzene, quite free from resinous matter, were formed, which had only to be pressed in filter paper to remove adhering amyl alcohol. The interaction is represented by the equation—



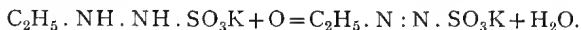
According to Pabst and Girard (Ger. Pat. 6,034), sulphanilic acid heated with lead chamber crystals yields the corresponding diazo-derivative.

Möhlau (Ger. Pat. 25,146) found that diazobenzene chloride was formed by the action of zinc dust (7 parts) on a cold solution of aniline nitrate (15.5 parts) in water (500 parts), when hydrochloric acid of sp. gr. 1.16 (34 parts) was added gradually—



The reaction is stated to be capable of general application.

The oxidation of hydrazines yields diazo-compounds. Thus Fischer (Ann. **199**, 302) prepared diazoethane potassium sulphite by adding excess of mercuric oxide to a concentrated solution of ethylhydrazine potassium sulphite, and filtering at once. By addition of alcohol and then ether he obtained the body in crystalline form—



6. Fatty Diazo-Bodies.—While nitrous acid transforms primary aromatic amines in acid solution into diazo-bodies, and in the absence of acid into diazoamido-derivatives, the fatty amines are in general hydroxylated without any intermediate diazo-compounds being produced.

Curtius (J. pr. Ch. **146**, 401) has found however that the esters of fatty amido-acids can be diazotised as easily as the members of

the aromatic series, and one of the results of this work has been the

isolation of hydrazoic acid $\begin{array}{c} \text{N} \backslash \\ \parallel \\ \text{N} / \end{array} \text{NH}.$

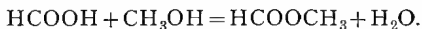
Thus diazoacetic ether is prepared by taking amidoacetic ether hydrochloride (50 gr.), which has been freed from excess of hydrochloric acid by heating in the water bath, placing it in a separating funnel of one litre capacity with just enough water to dissolve it, an operation which at once lowers the temperature of the mixture to 0° , and adding a concentrated solution of sodium nitrite (25 gr.). When pure materials have been used no diazoacetic ether is formed at this stage. But as soon as dilute sulphuric acid is added drop by drop, a gradual rise in temperature is observed, and the liquid becomes turbid. Oily yellowish drops begin to collect on the surface, and soon a layer of oil would form. It is better however to extract the liquid at once with ether before this takes place. The ethereal layer is removed, and more sulphuric acid added, and this process is continued as long as any milkiness is produced by the addition of fresh acid. The diazoacetic ether is then separated from the ether, care being taken to avoid bringing its explosive properties into play.

CHAPTER XIV

PREPARATION OF ESTERS

By esters we mean ethereal salts of acids. They may be regarded as alcohols in which the hydrogen of the hydroxyl group has been replaced by acid radicals, or as acids in which the hydrogen of the carboxyl has been replaced by alcohol radicals.

1. Action of Hydrochloric Acid on the Free Acid and an Alcohol.—Esters are frequently made by conducting dry hydrochloric acid into a solution, if necessary a warm solution, of an acid in an alcohol. Thus in the case of formic acid and methyl alcohol the powerful attraction of the hydrochloric acid for water produces the ester in accordance with the equation—



From dibasic acids, acid esters can be prepared in this manner.

As nearly all esters are insoluble in water, they are separated by pouring the mixture, which has been saturated with hydrochloric acid and allowed to remain at rest for some time, into a considerable volume of water. The ester appears as an oily layer. If the ester is somewhat soluble, the liquid must be extracted with ether. The addition of potassium carbonate to the water assists the extraction, as the esters are much less soluble in a strongly alkaline solution.

The oily layer is in most cases fractionally distilled, as the esters, excepting when they have large and complicated formulæ, can usually be distilled unchanged under the ordinary pressure of the air.

Exceptions to this rule are very uncommon. A decomposition like that of isopropyl benzoate into benzoic acid and propylene (Linnemann, Ann.

161, 15) is so rare that, in this case, it serves as a test for isopropyl alcohol. Equally unusual is the quantitative decomposition of laevo-rotatory methyl malate into methyl fumarate and water (Anschütz and Bennert, Ann. **254**, 164).

When the acid is a solid it is never completely converted into ester by this process, so that the oil, precipitated on addition to water, has to be washed with an alkaline solution to remove unchanged acid. If the latter is left mixed with the ester it separates during the distillation as a solid, and its presence is apt to lead to the cracking of the flask.

Anschütz and Pictet (Ber. **13**, 1,175) have drawn attention to the fact that many esters are partially saponified by contact with water. Thus it is impossible to obtain the esters of tartaric and racemic acids in neutral condition by this method. The pure esters are obtained by direct fractionation of the mixture, saturated with hydrochloric acid, *in vacuo*. Recourse may also be had to some other reaction, such as that involving the use of the silver salts.

The formation of the esters here depends on the abstraction of water by the hydrochloric acid. The water produced by the action itself necessarily accumulates and so interferes with the final completeness of the chemical change. It stands to reason therefore that, as Anschütz and Pictet (Ber. **13**, 1,176) have shown, the more perfectly this is removed the more nearly will the yield of ester approach the theoretical.

Their procedure was as follows: The powdered tartaric acid was covered with an equal weight of methyl, ethyl, or propyl alcohol, and, after the cooled mixture had been completely saturated with hydrochloric acid gas, was allowed to remain at rest for at least twenty-four hours. The liquid was then decanted from a small quantity of undissolved acid, a stream of dry air was drawn through it, and then the alcohol and aqueous hydrochloric acid were removed by heating on the water bath under considerably diminished pressure. In accordance with the above principle a fresh quantity of alcohol was next added to the residue, and the whole once more saturated with hydrochloric acid. Finally the mixture was fractionally distilled under diminished pressure. The yield was 70 per cent. of that theoretically possible.

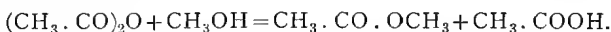
In rebuttal of the statement that this general method was not applicable to the case of oxyglutaric acid (Ber. **24** 325), they showed that the ester

could easily be obtained as a liquid boiling at 150° under a pressure of 11 mm. (Ber. **25** 1926).

It is true that some acids, which are soluble with difficulty in alcohol, are less easy to convert into esters by this method. Terephthalic acid (Ann. **245**, 140) is a case in point. When this difficulty arises it is better to use the acid chloride to start from (cf. § 10).

2. Preparation of Esters from Anhydrides and Alcohols.—

By boiling anhydrides of acids with alcohols we obtain the esters of the acids. Thus acetic anhydride and methyl alcohol give methyl acetate—



Under the same circumstances the anhydrides of dibasic acids, such as succinic acid, give the corresponding acid esters (Heintz, Pogg. Ann. **108**, 82; cf. Crum Brown and Walker, Ann. **261**, 117).

3. Action of Sulphuric Acid on the Free Acid and an Alcohol.—This method is less often used than that of distilling a mixture of a salt with an alcohol and sulphuric acid. Yet Markownikoff (Ber. **6**, 1,177) has shown that, just as in the case of Boullay's method of preparing ether, here a relatively small amount of sulphuric acid is capable of transforming a large quantity of a mixture of an acid and an alcohol into the corresponding ester. He heated the sulphuric acid in a retort to 130° , and allowed a mixture of molecular proportions of alcohol (93 per cent.) and acetic acid to flow slowly into it. By using sulphuric acid (10 gr.), acetic acid of sp. gr. 1.065 (50 gr.), and alcohol (38 gr.), he obtained acetic ether (70 gr.) in four hours. The sulphuric acid could be used over again, and the same sample gave eventually 232 grams of crude acetic ether.

This method can also be used for preparing the esters of dibasic acids, but their high boiling-points prevent the process being continuous. The yields, however, are very good, for succinic acid (20 gr.), alcohol (8 gr.), and sulphuric acid (1 gr.), after being boiled together for two hours with a reflux condenser, produced 25 grams of succinic ether, the theoretically possible quantity being 28 grams. The ester is separated as before by pouring the product into water.

Böttiger (Ber. **14**, 317) evaded the hydrolytic effect of the water as follows: He mixed equal volumes of pyruvic acid and alcohol, cautiously added half a volume of concentrated sulphuric acid, and

after the mixture had become cold, poured it into a layer of ether floating on water. The pyruvic ether, which is so easily hydrolysed that on standing for a short time in contact with water it is completely decomposed, was separated from the ether by spontaneous evaporation of the latter.

The same observer (Ber. **13**, 2,345) found that, when α -oxyvitric acid was dissolved in methyl alcohol and concentrated sulphuric acid was added drop by drop the acid was partially precipitated. When the mixture was heated to 50° , however, the mass became fluid again, and the ester was formed in the normal manner. Hougouneng (Bull. Ch. **45**, 328) obtained results diverging from Markownikoff's in so far that he found actions of this nature were often completed in a very short time. Thus by boiling molecular proportions of monochloroacetic acid and amyl alcohol with a small amount of sulphuric acid for a few minutes and then pouring the product into water, he obtained the ester of the acid very expeditiously.

Occasionally an acid is itself prepared in solution in concentrated sulphuric acid. In such cases the solution can be poured directly into alcohol without first isolating the acid. Thus when citric acid is dried at 150° , and heated on the water bath with two parts of concentrated sulphuric acid, carbon monoxide is given off, and acetone dicarboxylic acid (Ger. Pat. 32,245) remains behind. This loss of carbon monoxide is a common property of many α -oxy-acids (Ann. **264**, 262). To prepare the ester the mass is poured directly into thoroughly cooled absolute alcohol, and the mixture is allowed to remain for twelve hours. The liquid is finally diluted with a solution of common salt and extracted with ether ten times.

4. Action of Sulphuric Acid on an Organic Salt and an Alcohol.—Although the above method is very successful, salts of organic acids are more frequently used than the acids themselves. As a matter of course the salt is invariably used when it is more easily obtained than the free acid. The yields by this method are very good.

The method may be illustrated by citing the preparation of propyl butyrate. Pierre and Puchot (Ann. **163**, 272) mixed dry potassium butyrate (378 gr.) in small pieces with propyl alcohol, and added to it, with constant stirring, concentrated sulphuric acid (295 gr.) in small portions at a time. When rather more than three quarters of the acid had been added the mixture began to boil, and at the same time separated into two layers, an upper ethereal one, and a lower one containing potassium sulphate. When the

sulphuric acid had all been used the mixture was allowed to cool, and water was added. 382 grams of the ester, about 98 per cent. of the theoretical amount, were obtained.

If the liquid fails to boil of its own accord, as in making butyl valerianate (Ann. **163**, 285), it is heated to a temperature near the boiling-point for forty minutes. The yield here is 97 per cent. of the theoretical.

In making ethyl malonate, Conrad used the calcium salt of the acid. He first boiled sodium chloracetate with potassium cyanide. By adding the requisite amount of caustic soda and further boiling, sodium malonate was produced. He then neutralised with hydrochloric acid, and precipitated the calcium salt of the organic acid. Finally the salt was dried at 150°, mixed with four times the calculated amount of absolute alcohol and a quantity of concentrated sulphuric acid equivalent to the calcium, and heated in a water bath for twenty-four hours. After filtering, to remove the calcium sulphate and distilling off the alcohol at 100°, the ester was separated by addition of water. The yield was from 40 to 50 per cent. of the theoretical.

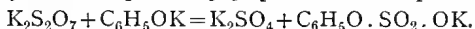
This method of preparing ethyl malonate has been superseded by that of Claisen and Crismer (Ann. **218**, 131). By mixing the cyanacetate of potassium, got by the action of potassium cyanide on potassium chloracetate, with alcohol, and conducting hydrochloric acid gas into the mixture, the saponification of the nitrile is combined with the transformation into the ester (cf. Backunts and Otto, Ber. **9**, 1,590), and a much better yield of the ester is obtained in a very simple manner.

5. Preparation of Esters of Inorganic Acids in Presence of Sulphuric Acid.—Processes similar to the above are used also for the preparation of esters of inorganic acids. Thus, according to Witt (Ber. **19**, 915), the simplest way of preparing ethyl, isobutyl, and amyl nitrites is by mixing sodium nitrite with a slight excess of the alcohol and adding dilute hydrochloric acid to the cold mixture. Ethyl nitrite comes off in gaseous form and can be washed, dried, and condensed by cooling. The higher homologues appear as oily layers, which can be separated and rectified. In all cases the yield of nitrite is nearly quantitative.

6. Use of Bisulphate and Pyrosulphate of Potassium.—For certain purposes acid salts of sulphuric acid can take the place of the acid itself. Thus phenol (9 parts), methyl alcohol (3 parts), and potassium bisulphate (14 parts) heated in a sealed tube for a few hours at 150°, give anisol, the methyl ether of phenol.

Sulphates of phenol radicals may be obtained by the action of potassium pyrosulphate. Baumann (Ber. **11**, 1,907) used the

following method for obtaining them. Phenol (100 parts), potassium hydroxide (60 parts), and water (80 parts) were mixed in a large flask. As soon as the mixture had cooled to 60–70°, finely powdered potassium pyrosulphate was gradually added. The mixture was kept at 60–70°, a temperature which must not be exceeded, for eight to ten hours, and frequently shaken. At the end of that time the interaction was complete, and the contents of the flask were extracted with boiling 95 per cent. alcohol, and the extract filtered while warm. On cooling, the solution deposited crystals of phenyl potassium sulphate. Although this salt is not very stable the yield was equal to 25–30 per cent. of the phenol taken—

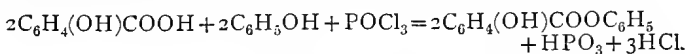


The sulphates of oxy-acids can be prepared in the same way. Thus salicylic acid (10 parts) is mixed with caustic potash (8 parts) and water (25 parts), and powdered potassium pyrosulphate (17 parts) is gradually added to the warm mixture, which is continually agitated during the process. After remaining at rest for some hours the mass is extracted with twice its volume of boiling 90 per cent. alcohol. On filtering the extract and adding an equal volume of ether, a thick liquid containing the salt separates out. This liquid is dissolved in a small amount of water, neutralised with acetic acid, and alcohol is then added until a permanent turbidity is produced. After a short time crystals of the potassium salt of the sulphuric ether of salicylic acid appear. The quality of the potassium pyrosulphate seems to have an important influence on the success of the action.

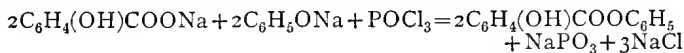
7. Use of Phosphorus Oxychloride in Preparing Phenyl Esters.—Nencki (J. pr. Ch. **133**, 282) made the important observation that the energetic action of phosphorus oxychloride on water could be used with advantage in the preparation of phenyl esters. According to Seifert (J. pr. Ch. **139**, 467), almost quantitative yields and pure products can be obtained by using a sufficient, but not too great, excess of the oxychloride, and working slowly at a low temperature. A mixture of equal parts of formic acid and phenol were warmed to 80°, and treated gradually with phosphorus oxychloride ($\frac{1}{3}$ mol.¹). The fluid product was poured into a cold dilute solution of carbonate of soda, when the evolution of hydrochloric acid had ceased, and the oil which separated was rectified *in vacuo*.

¹ Probably a half molecular proportion would be better.—[Author.]

Using Seifert's method a yield of 92·5 per cent. of salol (phenyl salicylate) can be obtained—

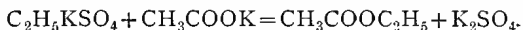


The free metaphosphoric acid produced by the action gives an opportunity for the formation of phenyl esters of phosphoric acid, and when a metal is present which can convert this into a salt, the yield is much improved. By using the sodium or other salts, both of the phenol and the acid, the yield is increased and the equation takes the form—



The operation is carried out by melting the sodium salts with phosphorus oxychloride or pentachloride. The temperature is not stated in the original papers. Seifert used 135° for the preparation of salol.

8. Action of Salts of Ethyl Sulphate on Organic Salts.—The salt of ethyl sulphate is dissolved in water or alcohol, and a solution of the organic salt is added. The mixture is heated in hermetically sealed vessels, if necessary, and finally distilled or extracted with ether. The following equation represents an action of this type—



Salts of phenols act in a similar manner. Thus Weselsky and Benedikt (M. f. Ch. **1**, 91) prepared the ethyl ether of resorcinol by boiling on the water bath, in a flask connected with an upright condenser, a mixture of resorcinol (200 gr.), caustic potash (400 gr.), and potassium ethyl sulphate (800 gr.), with enough alcohol to make the whole into a thin paste.

Hlasiwetz and Habermann (Ann. **177**, 340) obtained the monomethyl ether of quinol by heating quinol (10 gr.), potassium methyl sulphate (15 gr.), and caustic potash (6 gr.), for six hours in a sealed tube at 170°. An attempt made by Habermann (M. f. Ch. **5**, 228), however, to obtain the diethyl ether of alizarine, using the calculated molecular proportions of the reagents, gave only a small yield of the product.

In this case, as in others, the silver salts probably give better results than those of potassium. Brasch and Freyss (Ber. **24**, 1,961)

report, for example, that the silver salt of nitrocresol reacts smoothly with methyl iodide at the ordinary temperature, while the potassium salt fails to act even in the boiling mixture. Even in the case of the latter, interaction can be brought about by heating in a sealed tube for four hours at 100° .

Brühl (Ber. **24**, 3,376) prepared menthyl ethyl ether, $C_{10}H_{19}OC_2H_5$, by dissolving menthol (50 gr.) in dry toluene (30 gr.), adding sodium (8 gr.), and heating with a reflux condenser in an oil bath. At the end of fifteen hours the unattacked sodium was removed, excess of ethyl iodide was added to the solution, and the mixture was heated in the oil bath until it ceased to show an alkaline reaction. The sodium iodide was removed with water, the liquid dried again, the toluene and ethyl iodide distilled off, and the residue fractionated *in vacuo*.

9. Action of Alkyl Halides on Organic Salts.—As a rule the salts are covered with ether or alcohol, and the halide, usually diluted with ether, is added. Bromides frequently give better results than iodides. Silver salts are more often used than any others, although occasionally other salts are preferable. The mixtures are heated with an inverted condenser, or in a sealed tube.

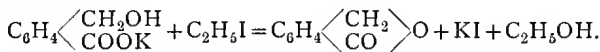
The difference between the actions of salts of different metals is exemplified by experiments of Strecker and Fischer. The former (Ann. **118**, 172) heated argento-xanthine with methyl iodide, and obtained a methylxanthine, which was not identical with theobromine. The latter (Ber. **15**, 454), on the other hand, used the crystalline lead compound in place of the amorphous silver one, and found that theobromine was produced under these conditions. The salt was dried at 130° , and heated at 100° in a sealed tube for twelve hours with $1\frac{1}{4}$ parts by weight of methyl iodide. The interaction was almost quantitative, and the contents of the tube formed a nearly dry mass, coloured strongly yellow by the lead iodide produced by the action. The product was extracted with water and a small amount of dissolved lead precipitated from the filtrate with hydrogen sulphide. On adding excess of ammonia and evaporating, the theobromine separated out.

Seidel (Ber. **25**, 431) states that the silver salt of fulminuric acid is hardly affected by ethyl iodide when the mixture is boiled with a reflux condenser. He finds, however, that on heating these substances for a few minutes in a sealed tube at 80 – 90° , the change into the ester, $C_3H_2N_3O_2(OC_2H_5)$ is quantitative (cf. Nef. Ann. **280**, 334).

Potassium salts are frequently employed. They are not prepared directly, but are formed by neutralising the acid with the calculated amount of potassium hydroxide or carbonate. The further treatment is the same as in the case of silver salts.

After a number of vain attempts Ladenburg (Ber. **25** 2,771) found the following was the only way of preparing the ester of nipecotinic acid. Equimolecular quantities of the hydrochloride of the acid and sodium carbonate were evaporated in water solution, and the residue was dried at 130° . The resulting brown hygroscopic mass was pulverised in a warm mortar, and heated in a sealed tube at 100° for 5 to 6 hours with a molecular proportion of methyl iodide. The product was extracted with absolute alcohol, and the alcohol was driven off by dilution with water and evaporation. The liquid was then shaken with freshly precipitated chloride of silver. On adding mercuric chloride to the filtrate an insoluble double salt was formed, which was finally decomposed with hydrogen sulphide. The filtrate gave on evaporation crystals of the hydrochloride of the methyl ester of nipecotinic acid, having the formula $C_5H_9O_2CH_3NH.HCl$.

It is seldom observed that actions of the present nature follow an *abnormal course*. In this connection Hjelt (Ber. **25**, 525) states that when the potassium salt of benzyl alcohol *o*-carboxylic acid is warmed in alcoholic solution with ethyl iodide, phthalid is formed on account of the instability of the ester.



Sodium salts can also be used, and are often preferred for manufacturing purposes on account of their cheapness. Thus the ethyl ester of rosaniline sulphonic acid may be prepared by heating the sodium salt (10 kilos.), water (50 l.), alcohol of sp. gr. 0.830 (50 l.), and caustic soda of sp. gr. 1.38 (750 gr.), with ethyl iodide (1.3 kilos.) in a vessel attached to a condenser till the liquid has changed its colour from yellowish-brown to violet-red. At this point fresh portions of the same amounts of caustic soda and ethyl iodide are added, and this process repeated each time as soon as the change in colour has taken place. The total amount of caustic soda used is 4.5 kilos., and of ethyl iodide 7.8 kilos.

It may be well to give also the method of recovering the iodine, as the necessity for doing this frequently arises in the laboratory. When the action is completed, the product is neutralised with hydrochloric acid, the alcohol is distilled off, and excess of sulphurous acid is added to the cold residue. After remaining for twelve hours the liquid becomes almost colourless, and the iodine can be precipitated as cuprous iodide.

10. Action of Acid Chlorides on Alcohols.—Just as alkyl halides interact with salts giving esters, so, inversely, the same

products are obtained by the action of acid chlorides on potassium or sodium alcoholates. The alcoholate is diluted with alcohol and the acid chloride is added. This general method is seldom departed from, although Emery (Ber. **22**, 3,185) prepared methyl succinate by the action of succinyl chloride in ethereal solution on dry sodium ethylate.

Acid chlorides are so energetic in their action, however, that esters may be obtained by simply pouring them into alcohols, hydrochloric acid being given off. This process is so satisfactory that acids might advantageously be converted into esters, by way of the chlorides, more frequently than is actually the case. It has already been shown that terephthalic acid cannot conveniently be made into the ester with the help of hydrochloric acid. Baeyer (Ann. **245**, 140) obtained a good yield of the methyl ester, however, by warming the powdered acid with the calculated amount of phosphorus pentachloride in the water bath till it was completely dissolved, and then pouring the product into excess of methyl alcohol. The methyl ester was insoluble in the alcohol and soon separated itself from the latter. Rupe (Ann. **256**, 7) prepared the methyl ester of dichloromuconic acid in the same way. Here too the most of the ester deposited itself directly, and the rest was precipitated by adding water.

Benzoyl chloride has an unusual capacity for forming esters (Baum, Z. physiolog. Ch. **9**, 465). Even in aqueous solutions of alcohols, provided they are first rendered alkaline, the esters are formed at once and are easily separated, as they are usually quite insoluble in water.

The carbohydrates likewise give benzoates in the presence of water. Thus Baumann (Ber. **19**, 3,219) dissolved grape sugar (5 gr.) in water (15 cc.), added 10 per cent. caustic soda (210 cc.), and shook the mixture with benzoyl chloride (30 cc.) until the odour of the latter was no longer perceptible. The total product was 13 grams, and consisted chiefly of the tetrabenzoate.

The sulphonic chlorides act in the same way as ordinary acid chlorides, only less energetically. Schiaparelli (Jahresb. **1881**, 539) suggests the addition of zinc dust or zinc chloride to assist their action.

11. Preparation of Ethers by the Action of Alcoholic Caustic Potash on Chloro-Derivatives.—Alkyloxy-derivatives can frequently be made by the action of alcoholic caustic potash on chloro-derivatives. For example, Willgerodt (Ber. **12**, 762) has investigated the action of solutions of caustic potash in various

alcohols on α -dinitrochlorobenzene, and obtained ethyl, allyl, phenyl, and other ethers. Thus he dissolved α -dinitrochlorobenzene in methyl alcohol, added slowly a solution of caustic potash in methyl alcohol, and agitated the mixture continuously. The interaction proceeded smoothly, and by distilling off the alcohol and recrystallising from alcohol he obtained the pure methyl ether. In another experiment he dissolved the same chloro-derivative in glycerol, in which it was only soluble with difficulty, added the solution of caustic potash in the same solvent, and so prepared the mono- α -dinitrophenyl ether $C_6H_3(NO_2)_2.O.C_3H_5(OH)_2$. In all cases an excess of alkali is to be avoided, as it is apt to produce saponification.

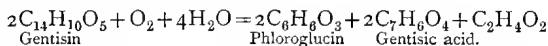
12. Preparation of Salol.—An exceptional case is that of salicylic acid, which turns quantitatively into salol when heated alone at $160-240^\circ$. Provision must be made for the removal of the water formed, and access of air is prevented as far as possible. The behaviour of other oxy-acids whose constitution would favour such a transformation seems not to have been investigated.

It may be mentioned, in concluding this chapter, that some esters decompose into resinous material on short exposure to the air. The methyl ester of $\Delta^{1.5}$ dihydrotetraphthalic acid (Ann. **258** 18) is a case in point.

CHAPTER XV

FUSION WITH CAUSTIC ALKALIS

1. Description of the Apparatus and Method.—The fusion of organic bodies, such as sulphonic acids, resins, etc., with caustic alkalis, is a method in frequent use for obtaining well-defined decomposition products. For example, Hlasiwetz and Habermann (Ann. **175**, 62) found that gentisin was decomposed by its means in accordance with the equation—



Gentisic acid was later identified as quinol carboxylic acid.

Fusion with potassium hydroxide does not require so high a temperature as that with sodium hydroxide, but the actions of the two are not always identical. The temperature at which the operation is conducted also frequently affects the result.

The method has been almost invariably to melt the substances in a silver basin over the naked flame. A better plan is suggested by Liebermann (Ber. **21**, 2,528). He employs nickel basins, and heats them on a copper bath shaped like Victor Meyer's drying baths (Fig. 39). The bath can be charged with naphthalene, anthracene, anthraquinone, or other substance of high boiling-point. When carried out under these conditions the fusion requires neither stirring nor other attention. Anthraquinonesulphonic acid can be fused with caustic potash at the temperature of boiling naphthalene. For anthracenesulphonic acid this temperature is too low, and anthracene vapour must be used. Boiling anthraquinone need only be employed in extreme cases.

When the substance is soluble in water it is dissolved in as little of the solvent as possible. Then the caustic potash and sometimes a little more water are added. As much as fifteen times their weight of alkali is used with some substances.

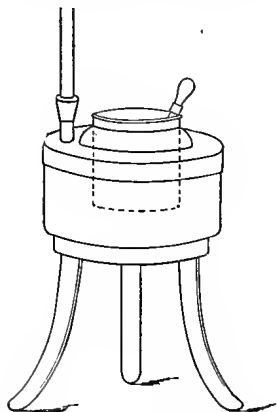


FIG. 39.

The following apparatus (Fig. 40) has been found by the author to be serviceable in most cases. A rather large test tube (3.3 cm. \times 30 cm.) passes through a hole in a flat cork which rests on the rim of a larger tube of Jena glass (4.5 cm. \times 35 cm.), which serves as a mantle. Substances of known boiling-point are placed in the outer tube so as to fix the temperature at which the melting takes place. Even at 250° the inner tube is not attacked by the fused alkali. The convenience of the apparatus lies in the fact that 100 grams of the mixture can be operated on at one time,

the progress of the action can be easily observed, the gases which are evolved can be readily collected, and the apparatus is more easily handled than a basin. Silver or nickel basins need therefore only be resorted to when large quantities of material have to be worked up at one operation.

Heumann's synthetic preparation of indigo (Ber. **23**, 3,434) affords a good example of a fusion. Amidophenylacetic acid (1 part) was melted with potassium hydroxide (3 parts) and water (1 part). The mass became yellow about 180–200°, and later the colour became fiery reddish-yellow, and the heating was continued until the colour ceased to deepen. The substance was then allowed to cool, and was dissolved in water (200 parts), and air was drawn through the solution until all the indigo-white was converted into indigo.

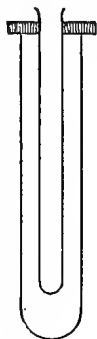
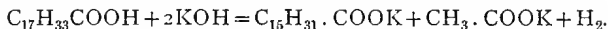


FIG. 40.

It is frequently possible, although not always so convenient in the laboratory, to carry out actions of this class with dilute alkalis in sealed

tubes. For example, dimethyl- α -naphthylaminesulphonic acid (one part), when melted with caustic soda (two parts), and water (one part), for half an hour at 280—290°, yields dimethyl- α -amidonaphthol. But the action is just as successful if more dilute alkali is used and the operation is conducted in a hermetically sealed tube. Similarly Roemer and Schwarzer (Ber. **15**, 1,401) prepared isoanthraflavic acid by heating β -anthraquinonedisulphonate of sodium with a solution of caustic potash, and found that under these conditions of temperature and concentration less isopurpurin was formed than under any other circumstances.

2. Oxidation accompanies the Fusion.—When the temperature is high enough one effect of fusing is always to produce oxidation with evolution of hydrogen gas. Many years ago Varrentrapp (Ann. **35**, 196) found that on fusing oleic acid, palmitic acid and acetic acid were formed according to the equation—

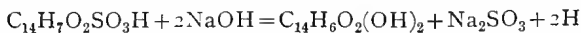


Barth and Schreder (Ber. **12**, 418) state that when phenol is melted with six times its weight of sodium hydroxide the sodium phenolate melts and floats on the surface as an oily layer. Gradually, however, a slight frothing due to the evolution of hydrogen becomes visible. This increases, and the fluid becomes brown till finally it turns into a homogeneous spongy mass. When this stage has lasted some time, and the froth has begun to subside, the flame is removed. The substance, when cold, is thrown into dilute sulphuric acid and the solid matter separated by filtration. On extracting the filtrate with ether a quantity of trioxybenzene is obtained (20 per cent. of the phenol used), which consists chiefly of phloroglucinol. The effect is therefore here to oxidise the phenol. The fused mass is almost invariably worked up in the manner described.

Tiemann and Reimer (Ber. **10**, 1,568) transformed aldehydosalicylic acid almost quantitatively into phenol dicarboxylic acid by gentle fusion with caustic potash. They used from ten to fifteen times as much of the alkali as of the acid and a little water in addition. The fusion lasted only 6–8 minutes. On dissolving the fused mass in water and adding hydrochloric acid most of the product was precipitated, and the rest was separated by extraction with ether.

3. Promotion and Restraint of Oxidising Influence.—The hydrogen which is evolved naturally has a tendency to undo part

of the oxidising effect of the fusion with alkalis. Thus, in preparing dioxyanthraquinone from anthraquinonesulphonic acid and sodium hydroxide, the nascent hydrogen produced by the action—



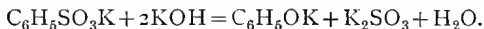
partially reduces some of the dioxyanthraquinone, or even reconverts it into anthraquinone. Koch's discovery was therefore an important one when he found that this reversal of the action could be avoided by *introducing oxidising agents* into the fusing mass. He found that potassium chlorate was the best substance, and that the yield of alizarin became almost quantitative when it was employed—



In the manufacturing process a little water is added, the fused mixture is kept at 160–170°, and is constantly stirred. The operation occupies from two and a half to three days.

If this action is compared with the last example, the oxidation of aldehydosalicylic acid, it will be observed that bodies with complex aromatic rings are more readily attacked than simple benzene derivatives.

When the substances taking part in the action are not appreciably attacked by the nascent hydrogen, good yields may be obtained without the addition of oxidising agents, provided the other conditions are favourable. Thus Degener (J. pr. Ch. **128**, 300) found that when benzenesulphonate of potassium was heated at 252° with six molecular proportions of potassium hydroxide, the yield of phenol was 96 per cent. of the theoretically possible amount—



When it is desired to *restrain* the oxidising effect of the operation, iron filings are frequently added to the fusing mass.

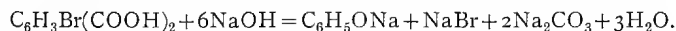
4. Differences between the Action of Sodium and Potassium Hydroxides—A striking illustration of the difference between potassium and sodium in their effects on organic actions may be found in Kolbe's synthesis of salicylic acid. Sodium phenolate gives salicylic acid, while potassium phenolate yields *p*-oxybenzoic acid.

Barth and Schreder (Ber. **12**, 422) found that by continuous heating of benzenetrisulphonic acid with caustic potash, first one

sulphonic acid group, then a second was replaced by hydroxyl, but that efforts to replace the third by further raising the temperature led only to the almost complete combustion of the whole substance. Fused caustic soda, on the other hand, acts with ease and gives 25-30 per cent. of phloroglucinol (trioxybenzene).

5. Differences in Result under Different Conditions.—According to Gürke and Rudolph, when naphthalene trisulphonate of sodium is heated with half its weight of caustic soda and an equal amount of water for several hours at 170-180° in an oil bath, a mixture of naphtholdisulphonic acids is obtained. The operation must be conducted in closed vessels to avoid loss of water and consequent drying of the mixture. If naphthalenetetrasulphonate of sodium (10 parts) is dissolved in as little water as possible, mixed with caustic soda (6 parts), and heated in closed vessels at 180°, the sodium salt of naphtholtrisulphonic acid is formed. But if the temperature is raised to 250° this substance is transformed into the corresponding salt of dioxynaphthalenedisulphonic acid.

Fischli (Ber. **12**, 621) found that when bromoterephthalic acid was fused for some time with sodium hydroxide, sodium phenolate was produced—



But when he modified the action by adding the acid to the molten alkali and letting the mass cool at once, a large amount of oxyterephthalic acid was formed.

6. Fusion of Calcium and other Salts with Alkalis.—Calcium salts may be used in fusions instead of those of potassium and sodium. For example, Weber (Ber. **14**, 2,206) dissolved α -naphthalenedisulphonate of calcium in a little water in a rather large flask, added two and a half times as much caustic soda, and stirred the mass while heating it up to 290-300°. By conducting hydrogen into the flask the air was displaced, the substance remained white, and pure dioxynaphthalene was formed.

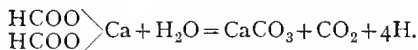
Lead salts have occasionally been fused with caustic potash.

7. Reduction of Nitrophenols.—It has been established as a general action by Weselsky and Benedikt (Ber. **11**, 398) that mononitrophenols give azophenols on fusion with caustic potash. For example, *o*-nitrophenol is thrown into 4-6 times its weight of potassium hydroxide fused with a little water. The mixture

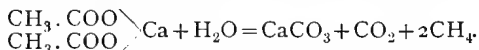
is at first coloured red by the nitrophenolate of potassium. The heating is stopped as soon as the mass has acquired a dark-green colour and a metallic lustre and begins to give off ammonia. The fused substance becomes dark-red again almost immediately, and is then dissolved in water. Sulphuric acid precipitates a solid, which is washed, dried, and extracted with ether. The latter deposits on evaporation pure azophenol. The yield is not mentioned.

8. Analogy of this Reaction to Putrefaction.—It may be worth while to draw attention to the fact that the unusual oxidation accompanied by evolution of hydrogen, which is brought about by fusion with alkalis, is quite analogous to the decomposition which organic substances, like albumen, undergo during putrefaction (Nencki, *J. pr. Ch.* **125**, 123, and Hoppe-Seyler, *P. Ar.* **12**, 1). Albumens in process of putrefaction give tyrosine, and Liebig (*Ann.* **57**, 127) obtained the same substance on fusing casein with caustic potash.

Similarly, in a simpler case, calcium formate decomposes according to the equation—



As is the case in fusions, the hydrogen acts as a reducing agent when it has opportunity. Thus calcium acetate decomposes according to the equation—



When putrefaction takes place in the air, the hydrogen set free by the chemical change combines with oxygen from the air. The atomic oxygen set free by this means from the molecules of the free gas then gives occasion to very complicated oxidations.

Hydrogen from solution in palladium also combines with oxygen, and for the same reason is able to produce oxidation of organic bodies (*Z. physiolog. Ch.* **2**, 22). Indeed, the oxygen obtained under such conditions is the most active form of the element that we know. Baumann (*Z. physiolog. Ch.* **5**, 244) has shown that it can convert carbon monoxide into carbon dioxide at the ordinary temperature, an effect which even ozone is incapable of producing.

CHAPTER XVI

PREPARATION OF HALOGEN COMPOUNDS

SECTION I.—BROMO-DERIVATIVES

IN most cases bromination is effected by the use of bromine itself, sometimes in presence of substances which assist its action.

Other agents, such as hydrobromic acid, bromides of copper, phosphorus and calcium, and potassium hypobromite, are also employed.

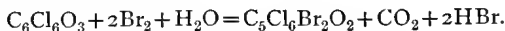
1. Bromine.—Commercial bromine is almost never pure. According to Reimann (Ber. **8**, 792), it may contain as much as 10 per cent. of impurities, of which bromoform is one of the most common (Ann. **95**, 211).

Gessner (Ber. **9**, 1,507) recommends repeated shaking with distilled water and subsequent distillation over concentrated sulphuric acid for the removal of chlorine. The first part of the distillate is rejected. Hydrobromic acid is removed by distilling over precipitated manganese dioxide or mercuric oxide (Ber. **13**, 1,338). Drying is managed by shaking with concentrated sulphuric acid or adding phosphorus pentoxide. If greater purity is required chemically pure bromine may easily be made by Stas' method¹ in pounds at a time.

Bromine is a much less active agent when dry than when moist. This is easily explained by a consideration of Thomsen's determinations (Ber. **5**, 770) of the heat given out by its union with hydrogen in each condition. For the former it is 8.4 cal., and for the latter 28.3 cal. Zincke and Kegel (Ber. **23**, 235) state, for example, that pure bromine will not act on hexachlorotriketone,

¹ Stas' "Nouvelles recherches sur les lois des proportions chimiques, etc." Brussels, 1865.

even when they are heated together at 100° for a considerable time. But when some water¹ is present carbon dioxide is evolved immediately, and hexachlorodibromoacetylacetone is formed according to the equation—



Bromine is sometimes used without dilution. In such cases it is mixed with the substance, and the excess is removed by evaporation on the water bath. For example, Jacobsen (Ber. **14**, 2,351) dissolved *m*-toluic acid in excess of bromine, and after twelve hours allowed the latter to evaporate. He brought the residue into solution by means of calcium carbonate, and by precipitation with hydrochloric acid obtained two monobromo-*m*-toluic acids.

Furil is not attacked by chlorine or bromine in chloroform solution, but by dissolving one part of furil in forty parts of previously cooled bromine, Fischer (Ber. **13** 1,338) obtained an addition product having the composition $\text{C}_{10}\text{H}_6\text{Br}_8\text{O}_4$.

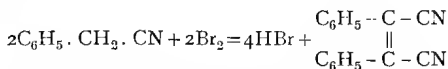
Paal (Ber. **17**, 2,760) obtained bromophenylmethylfurfurane tetrabromide, $\text{C}_{11}\text{H}_9\text{Br}_5\text{O}$, by dissolving phenylmethylfurfurane in excess of bromine (which was kept so cold that a part of it was frozen during the operation), allowing the bromine and hydrobromic acid to evaporate in the air, and recrystallising the residue.

Hermetically sealed tubes have frequently to be used, as bromine boils at 58° . It is often diluted in such cases (see below). Bischoff (Ber. **24**, 2,016) heated ethylsuccinic anhydride (36 gr.) with bromine (46 gr.) and chloroform (40 gr.) in tubes at 130 – 140° for five hours. At the end of this time the colour of the bromine had disappeared. The mixture was placed *in vacuo* to remove hydrobromic acid, and the chloroform was evaporated on the water bath. Bromoethylsuccinic anhydride remained.

Its power of combining is so great that it can often be added to substances which are heated to a high temperature and with which it combines rapidly in the act of being volatilised. This may be illustrated by the case of Greiff's dibromoanthranilic acid (Ber. **13**, 288). He allowed bromine

¹ The frequent necessity for the presence of water may be further illustrated by Nef's statement (Ann. **266** 70), that sodium has no action on phthalic, succinic, and other acids in absolute ethereal solution. Brühl (Ber. **25** 367) finds the same to be true of many alcohols like menthol and borneol.

to flow slowly into *o*-nitrotoluene at 170°. Hydrobromic acid was rapidly evolved and so much heat produced that no further heating from the outside was necessary for the quantity (200 gr.) of the substance used. After two atomic proportions of bromine had been added, the operation was interrupted, and the mass, which became crystalline on cooling, was treated with sodium carbonate. From the solution acids precipitated the dibromo-anthranilic acid which had been produced by molecular rearrangement. To further illustrate this way of applying bromine, the actions on benzylcyanide and ethylsuccinic acid may be mentioned. In the former case Reimer heated the substance to 170°. A violent reaction ensued as the bromine was slowly added, and stilbene dicyanide was formed according to the equation—



In the second case Bischoff (Ber. **24**, 2,015) melted 15 grams ethylsuccinic acid in a small flask, and as the temperature was gradually raised to 200°, he added 16 grams bromine through a funnel with a capillary stem.

Application in the form of vapour renders the action of bromine much less violent. The substance is brought in contact with the bromine under a bell jar. This method was used as early as 1836 by Péligot (J. pr. Ch. **8**, 258) for preparing bromobenzoic acid, as he found that the direct action on silver benzoate was too energetic. The substances stood side by side for twenty-four hours, and at the end of that time the bromobenzoic acid could be extracted by alcohol, while silver bromide remained behind. On the other hand, Kekulé (Ann. **117**, 122) attempted to make bromosuccinic acid in this way and failed. Silver bromide was formed indeed, but, on extracting the mass with water, nothing but unchanged succinic acid was obtainable.

Sometimes this method is varied by placing the substance in a tube and carrying the vapour of bromine over it by means of a stream of carbon dioxide. The bromine is placed in a small flask behind the tube, and the vaporisation can be accelerated by gentle warming. If the bromine is made by heating potassium bromide, potassium bichromate, and sulphuric acid, an application may be found in this way for the bromide which is formed as a by-product in so many actions.

Niementowski (Ber. **25**, 868) applied this method as follows:—200 grams of *o*-acetotoluide were dissolved in 1,300 grams of glacial acetic acid, and a stream of air laden with bromine was led through

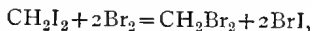
the solution until it had solidified to a mass of white crystals. After the mother-liquor had been removed by filtration and pressure the product was recrystallised once from alcohol, and gave 150 grams of chemically pure *m*-bromo-*o*-acettoluide. The mother-liquor contained considerable quantities of *m*-bromo-*o*-toluidine in consequence of the saponifying effect of the hydrobromic acid.

Actions like the present are usually *assisted by sunlight*, although in some cases exceptions to this rule must be recognised. For example, *o*-nitrocinnamic acid can be brominated, just like cinnamic acid itself, by adding it to liquid bromine or exposing it to bromine vapour. Yet Friedländer (Ber. **13**, 2,257) found that sunlight prevented the absorption of the vapour, for when the acid was exposed to the action of bromine in this form in bright sunlight, practically no increase in weight was observable. Special interest attaches to an observation of Wislicenus (Ann. **272**, 98) in this connection. He found that, when light is carefully excluded, angelic acid yields dibromoangelic acid, while the admission of light leads to the formation of the isomeric dibromotiglic acid. A thorough investigation of the influence of light on the progress of the action of halogens on aromatic compounds has been made by Schramm (M. f. Ch. **8**, 101).

The bromination of the side chains of aromatic hydrocarbons follows the rule given for their chlorination. Toluene itself is in this respect perfectly regular; but, according to Schramm (Ber. **17**, 2,922), its derivatives do not all show the same regularity. By the action of bromine on melted *p*-bromotoluene in molecular proportions he obtained *p*-bromobenzyl bromide in almost quantitative amount.

Bromine drives out iodine from many compounds and takes its place. For example, ethylene chloriodide is converted into ethylene chlorobromide.

Meyer and Müller (Ber. **15**, 1,904) found this method convenient for making isopropyl bromide since secondary propyl iodide is easily made, and bromine acts on it with great violence, replacing the iodine. The best result was attained by using one and a half times the theoretical amount of bromine. Henry (Ann. Ch. Ph. **30**, 266) made dibromomethane according to the equation—

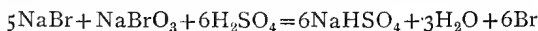


and removed the BrI with potassium hydroxide.

The addition of bromine to unsaturated bodies does not seem to

be always achieved with ease. At least Bennet (Ber. **12**, 656) could get no addition product with dichloroacrylic acid. It was obtained by Andrews (Ber. **14**, 1,679) by heating the acid to 100° with bromine (1 mol.). The almost colourless product of the reaction was the expected dichlorodibromopropionic acid. Henry, on the other hand (J. pr. Ch. **117**, 231), has made dipropargyl octobromide, $C_6H_6Br_8$, easily by addition of bromine to dipropargyl $CH \equiv C - CH_2 - CH_2 - C \equiv CH$. A case of a somewhat different kind is the formation of trimethylene bromide, where, according to Freund (M. f. Ch. **2**, 642), the addition of bromine to trimethylene is a slow process.

When *nascent bromine* is required, sodium bromide and bromate are added to the solution of the substance and the amount of sulphuric acid required by the equation—



is run in (Ger. Pat. 26,642).

Heinichen (Ann. **253**, 269) found that in making dibromosulphanilic acid, either from sulphanilic acid itself or from its barium salt, it was necessary to use nascent bromine in order to avoid the formation of tribromoaniline. The yield was almost equally excellent, whether he used a freshly prepared dilute solution of bromine in sodium hydroxide and allowed it to flow slowly into a solution of sulphanilic acid containing the requisite amount of hydrochloric acid, or mixed the sulphanilic acid with hydrobromic acid and added the calculated quantity of potassium bromate. He dissolved, for example, sulphanilic acid (17.3 gr.) in half a litre of water, added 43 per cent. hydrobromic acid (37.6 gr.), and with continual agitation allowed a solution of potassium bromate (11.1 gr.) in water (250 cc.) to flow in slowly. The experiment lasted thirty minutes, and the yield was 90 per cent. of the theoretical. When bromine and sodium hydroxide were used the yield even reached 95 per cent.

To restrain the too violent action of bromine a solvent such as ether, chloroform, glacial acetic acid, hydrochloric acid, carbon disulphide, or water, or a mixture of some of these, is employed. Less commonly alcohol, potassium bromide solution, hydrobromic acid, acetic ether, and other substances are used. It is not always a matter of indifference what solvent is taken, as the examples given below show.

On the other hand the substance to be acted upon is often dis-

solved in, or diluted with, a suitable medium. An excess of bromine is removed by heating, addition of sulphurous acid, or shaking with mercury.

It is generally found to be advantageous to use silver salts or esters instead of free acids for bromination.

The usual course is to drop the diluted bromine into the solution of the substance, or *vice versa*.

For example, bromanil is best made, according to Gräbe and Weltner (Ann. **263**, 32), by dissolving powdered paraphenylene diamine (10 gr.) in *glacial acetic acid* (40 cc.), warming slightly if necessary to bring about solution, and letting this solution, when cold, flow into a small flask surrounded by water and containing the bromine (40 cc.). The flow must be quite slow in order that as little bromine as possible may be driven off in the form of vapour. The resulting mass, which soon becomes solid, is stirred from time to time, allowed to stand over night, and is then warmed on the water bath till the evolution of hydrobromic acid and of unused bromine has ceased. The product is next mixed with water, and, after being warmed for a short time, is separated by filtration and thoroughly washed. After the oxidation with nitric acid (see Chap. XVII.) a yield of 30–32 grams of bromanil is obtained.

In brominating anhydro-pyrogallopropionic acid, Böttiger (Ber. **16**, 2,411) used as solvent a *mixture of glacial acetic acid and chloroform*. Acids containing three and five atoms of bromine were formed.

According to Schunk and Römer (Ber. **10**, 1,823) bromine has no action on flavopurpurin even when boiled with it in carbon disulphide solution. But when the substance is dissolved in boiling glacial acetic acid and bromine is added, the solution deposits on cooling needles of tribromoflavopurpurin.

Michael (Am. Ch. J. **5**, 203) showed that by dissolving one molecular proportion each of bromine and acetic acid in some *carbon disulphide*, and, with use of a reflux condenser, boiling till no more hydrobromic acid was given off, a yield of bromoacetic acid equal to 90 per cent. of the theoretical could be attained. Here, as in all cases of bromination, a small excess of bromine (about 5 per cent.) must be taken to make up for the part which is carried off along with the hydrobromic acid.

This method cannot be applied to homologues of acetic acid, but Michael (J. pr. Ch **143**, 92) found that it was effectual with

chlorides of such acids.¹ He heated the chloride, dissolved in a considerable amount of carbon disulphide, with rather more than the amount of bromine necessary to form the bromo-compound, until hydrobromic acid was no longer evolved. In this case the materials must be perfectly dry. When the brominated chloride is poured into water the bromo-acid, when into alcohol the bromo-ester, is obtained. For example, from 200 grams butyryl chloride Michael made nearly the theoretically possible amount of bromobutyric ether in ten hours' time.

As was discovered by Wolff (Ann. **264**, 233), *hydrochloric acid is a useful solvent* in brominating.

For example, a solution of three parts of levulinic acid in twelve parts of concentrated hydrochloric acid is cooled a few degrees below 0°, and to it is added drop by drop four parts of bromine in such a way that by continual shaking the latter is dissolved immediately. After the mixture has been kept at a low temperature until the red colour of the bromine has vanished, it is poured into much cold water. The whole is then filtered to remove any dibromolevulinic acid which may have separated out, and extracted with ether to obtain the monobromolevulinic acid. To purify the latter it is recrystallised from boiling carbon disulphide. When ether or chloroform is used as solvent instead of hydrochloric acid, the bromination goes too far, and almost nothing but the dibromo-derivative results.

In connection with this work, Gans succeeded in forming the previously unknown monobromopyruvic acid. He dissolved one part of pyruvic acid (b.-p. 165–170°) in four parts of concentrated hydrochloric acid, and added the necessary bromine, keeping the temperature meanwhile between 12° and 15°. This process is also the best for making the dibromo-derivative. To achieve this the requisite amount of bromine is taken and the temperature kept between 30° and 35°.

Many substances are brominated by merely *dissolving or suspending* them in water and adding bromine.

To illustrate this, the case of the three chlorobenzoic acids may be mentioned. Claus (Ber. **5**, 656) has shown that while the acids themselves are very variously affected by bromine, their bromo-derivatives are easily formed by adding bromine to warm solutions of their silver salts. Thus *o*-chlorobenzoic acid is scarcely attacked by bromine, even on prolonged heating in a sealed tube, while a warm solution of the silver salt in water

¹ In this connection see Volhard's method depending on the presence of phosphorus to be described later.

on addition of bromine gives *o*-chlorobromobenzoic acid in crystalline form on cooling.

The great difference which is sometimes found in the action of bromine when different solvents are used may be further illustrated by reference to a case examined by Baeyer and Bloem (Ber. **17** 996). They found that *o*-acetamidoacetophenone was brominated in the benzene ring in presence of water or acetic acid. But in chloroform or sulphuric acid (cf. M. f. Ch. **10**, 813) solution, or when bromine vapour was used, it acquired bromine both in the side chain and the ring, and *m*-bromo-*o*-acetamido-dibromoacetophenone was formed—



Alcohol can only be used as a solvent when bromine acts on the substance more rapidly than on the alcohol. Wallach (Ann. **227**, 280), in making tetrabromides of the terpenes, diluted 1 volume of the terpene with 4 volumes each of alcohol and ether, and added gradually 0.7 volumes of bromine. The tetrabromide being insoluble in alcohol was at once separated from the easily soluble oily by-products which were always formed at the same time.

Spitzer (M. f. Ch. **10** 110) made monobromopentamethylphloroglucinol by dissolving pentamethylphloroglucinol (2.5 gr.) in absolute methyl alcohol (23 gr.), and adding bromine (2.3 gr.) slowly to the cooled solution.

Kronfeld (Ber. **17** 716) found in a solution of bromine in potassium bromide the best agent for brominating amidonaphthoquinoneimide hydrochloride.

Bromine water, which, according to Slessor (New Edin. Phil. Jour. **7**, 287), contains at 5°, 3.6 per cent., and at 30°, 3.1 per cent. of bromine, is sometimes used for brominating. For instance, Fischer (Ann. **239**, 189) heated finely powdered dibromopyvureide with it in the proportion of 1 part to 20, and obtained on cooling tribromopyvurine. The yield was equal to 120 per cent. of the original substance.

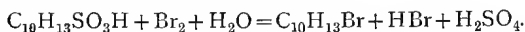
Many substances can be brominated quantitatively with dilute bromine water, and when the bromo-derivative is insoluble it comes out completely. Landolt (Z. physiol. Ch. **6** 184) determined the exact conditions, for example, under which phenol could be precipitated from solution in water as tribromophenol, and based thereon a method of quantitative estimation. Cresol is not precipitated quantitatively in the same way.

Acetic ether was used as a solvent by Pinner (Ann. **209**, 48). In trying to make bromo-derivatives of aldehyde he found that when the paraldehyde was dissolved in carbon disulphide or carbon tetrachloride no analysable products could be isolated, but by the use of twice its weight of acetic ether he obtained dibromo- and tribromo-aldehyde.

To make ethylene chlorobromide, James (Ber. **16** 79) dissolved bromine

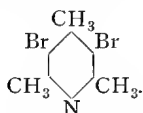
(200 gr.) in a mixture of equal parts of hydrochloric acid and water (1 kg.), and saturated the whole with chlorine gas at 0°. Ethylene was passed into this solution, and the oil which separated out was purified by distillation. He obtained 140 grams of ethylene chlorobromide.

An indirect mode of obtaining bromo-derivatives is that, first recognised as pretty general in its scope by Kelbe (Ann. **210**, 48), whereby *aromatic sulphonic acids are converted into brominated hydrocarbons*. By the action of bromine at the temperature of the water bath on 39.5 grams of *α*-cymenesulphonate of sodium, he made 28.5 grams bromocymene where 31.3 grams were theoretically obtainable—



This action goes the more easily, the stronger the action of bromine on the corresponding hydrocarbon itself is; so that its use is specially to be recommended where the latter action would be excessive in violence. The corresponding application of chlorine gives a less satisfactory result (Ber. **16**, 617).

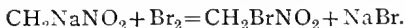
Two other *indirect methods* are worthy of mention. Pfeiffer (Ber. **20**, 1,345) found that collidine gave no substitution products with bromine, but that such compounds could be obtained from the potassium salt of collidine carboxylic acid. He dissolved the latter in three times its weight of water, and boiled it in a flask attached to a reflux condenser with twice its weight of bromine. A violent action ensued, and after a few minutes' further boiling, the excess of bromine was removed with sodium hydroxide. The oil which had separated out soon solidified to a mass of crystals, which gave on recrystallisation pure dibromocollidine—



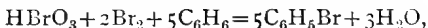
Lutidine dicarboxylic acid acts in a precisely similar manner. In the case of other acids of the group, such as *α*-*β*-pyridine dicarboxylic acid, the reaction goes less smoothly.

Many other substances do not yield bromo-compounds directly, although simple derivatives give them readily enough. To this class belong, for example, the fatty nitro-bodies. Thus bromine

does not attack nitromethane at all (Ann. **180**, 128), while it acts easily on sodium nitromethane, forming bromonitromethane—



The *hydrobromic acid*, which is given off in almost all the methods of bromination described, *is sometimes injurious*. When this is the case, it is frequently removed by passing a stream of air or carbon dioxide during the operation. The object is best attained, however, by adding potassium bromate, mercuric oxide, or lead oxide, a method similar, therefore, to that used in the case of iodine. The efficiency of the method has been tested by Krafft (Ber. **8**, 1,044). He took potassium bromate, bromine, and benzene in the proportions required by the equation—



and added sufficient sulphuric acid, diluted with twice its weight of water, to combine with the potassium. The reaction was complete after two hours, and the yield amounted to 70–80 per cent. of the theoretical.

When spontaneously inflammable bromoacetylene is evolved, the method given under chloroacetylene is employed.

2. Bromine Carriers.—These agents are similar to the more familiar chlorine carriers, and are very commonly used. Such substances are iodine, metallic iron, ferric bromide, ferric chloride, aluminium bromide (Ber. **25**, 797*c*), phosphorus, together with a few substances which have been used by their discoverers only. The most complete investigation of the subject has been made by Scheufelen (Ann. **231**, 52).

Iodine is added as such to the bromine, and considerably increases its activity. For example, Kolbe found that bromine did not act on carbon disulphide to produce a bromide even when the vapours of the two substances were passed through red-hot tubes. But Bollas and Groves (Ber. **3**, 508) heated carbon disulphide (2 parts) with bromine (14 parts) and iodine (3 parts) in an hermetically sealed tube for forty-eight hours at 150°, and on adding sodium hydroxide to the contents and distilling, obtained carbon-tetrabromide.

By the action of bromine on nitrobenzene, Kekulé (Ann. **137**, 172) obtained pentabromobenzene as the final product, but by using bromine (free from chlorine) to which a little iodine had been

added, and heating for 150 hours at 350–400°, Gessner (Ber. **9**, 1,507) obtained hexabromobenzene (see below).

Scheufelen (Ann. **231**, 164) obtained bromonitrobenzene, quite free from chlorine, by placing nitrobenzene (10 gr.), *ferric chloride* (2 gr.), and bromine (4.3 cc.), all carefully dried, in a tube and heating for twelve hours at 100°. On further heating, monobromonitrobenzene (14 gr.), ferric chloride (4 gr.), and bromine (11.2 gr.), for the same length of time at 75–80°, he obtained dibromonitrobenzene.

As is well known, bromine only acts on benzene after weeks of contact; but the same observer, by taking bromine (300 gr.), adding a few grams of ferric chloride to it, and allowing it to flow drop by drop into benzene (17 gr.), obtained 110 grams of hexabromobenzene, while the theoretical yield would have been 119 grams.

In connection with Scheufelen's work, Schiff (M. f. Ch. **10**, 39) made dibromobenzene, and obtained the ortho-compound in particular, as follows:—Paranitrobromobenzene (20 gr.) was heated in a sealed tube with the theoretically necessary quantity of bromine, together with enough excess of bromine to convert all the ferric chloride into bromide. The heating continued for fifty hours at 85–90°. The viscid contents of the tube were washed with water to remove iron salts, and by recrystallisation from alcohol a 90 per cent. yield of dibromonitrobenzene was attained. The nitro-group was replaced by hydrogen by first reducing with tin and hydrochloric acid, and then acting with ethyl nitrite, and *o*-dibromobenzene was the final product.

At Scheufelen's suggestion, Kerrow (Ber. **24**, 2,939) endeavoured to fix the limits of the action of chlorine and bromine carriers, and one of his results was the discovery that while the presence of one nitro-group greatly assists the introduction of halogens in place of hydrogen, more than one prevents it altogether. In such cases the nitro-groups themselves are more easily replaced by halogens than the neighbouring hydrogen atoms. But with the removal of the nitro-groups the influence of the halogen carriers reasserts itself, and the introduction of more halogen atoms progresses rapidly.

Ferric bromide (or the more easily prepared ferrous salt) has sometimes to be used in place of the chloride, because while up to 100° the chlorine of the carrier combines with the hydrogen to form hydrochloric acid, at higher temperatures such as 180° a part of the chlorine is likely to enter into the organic compound.

By using *iron wire*, Meyer and Müller (Ber. **24**, 4,249) avoided the difficulty sometimes caused by the chlorine of the chloride. They heated molecular proportions of ethyl bromide and bromine for an hour in a sealed tube with this agent, and found that, save for a small portion which remained unchanged, the substance had been converted completely into ethylene bromide.

Aluminium bromide is an excellent bromine carrier, transforming CCl_4 , C_2Cl_4 , and C_2Cl_6 , according to Gustavson (Ber. **14**, 1,709), into the corresponding bromine derivatives.

Blümlein (Ber. **17**, 2,486) threw aluminium (1 gr.) in small portions into carefully cooled bromine (150 gr.), an operation which was attended by a considerable evolution of light and heat, and, after the liquid had been cooled to 0° again, added α -naphthol. The excess of bromine was then driven off, and the resulting mass extracted with cumene. Pentabromonaphthol, $\text{C}_{10}\text{H}_2\text{Br}_5\text{OH}$, remained undissolved.

In a similar manner Ris (Ber. **20**, 2,621) added finely powdered β -dinaphthylamine to more than eight times the actually necessary amount of bromine, prepared as above by the addition of a little aluminium. A doughy substance was formed which, after being ground up with water, left as residue octobromo- β -dinaphthylamine, $\text{C}_{20}\text{H}_7\text{Br}_8\text{N}$.

The use of *phosphorus* as a halogen carrier was discovered by Corenwinder (Ann. Ch. Ph. **30**, 248), who made hydriodic acid by the action of water on phosphorus iodide. The application of red phosphorus instead of the yellow variety was first suggested by Personne (C. R. **52**, 468). The method is quite generally applied for the preparation of hydrocarbon bromides from alcohols.

The action takes place according to the equation—



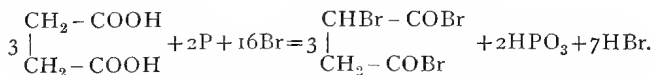
For example, in making ethyl bromide, red phosphorus is placed in a retort connected with a reflux condenser, and the proper amount of alcohol of at least 90 per cent. strength is poured over it. The calculated amount of bromine is added slowly. During this operation the retort must be cooled on account of the heat developed by the violence of the action. The ethyl bromide is finally separated by fractional distillation (cf. Ethyl iodide).

The ease with which *acids could be brominated in presence of phosphorus* was first pointed out by Hell (Ber. **14**, 891), and later Volhard (Ann. **242**, 144) showed what splendid results could be

attained by this almost forgotten method when used under proper conditions.

The prime condition necessary for the successful use of this way of brominating acids is that all the materials must be perfectly dry. As the red phosphorus usually contains some phosphoric acid, it must be washed with water until the washings cease to show an acid reaction, and once more dried.

The case of succinyl bromide will serve as a general example. The succinic acid and phosphorus are ground together in a mortar, and during the addition of the bromine the retort in which the mixture is placed is kept in motion to aid in mixing the ingredients. It is necessary to take a small excess of phosphorus and rather more bromine than the theory demands, as from 5 to 15 per cent. of the latter may be carried over mechanically by the hydrobromic acid. He describes in detail, as follows, the method of preparing the bromide of bromosuccinic acid. The action is expressed by the equation—



The reaction is best carried out in a tubulated retort, to whose neck a tube about 11 mm. in internal diameter, and 70 cm. in length is fused. This tube is inserted in a condenser jacket supplied with cold water. The upper projecting end of the tube is connected with absorption bottles to catch the hydrobromic acid. The connecting tube just passes through the cork of the first bottle and no more. Two bottles are used. They contain each a little water, and a tube reaching to the bottom of each connects them. This arrangement enables the liquid to pass from the one to the other, and yet excludes the possibility of its mounting back into the retort. Any escaping gases are carried by another tube into an open flask containing water, beneath the surface of which, however, the tube does not dip. Even when the evolution of hydrobromic acid and bromine is rapid, they are completely absorbed. The movements in the two bottles give an indication of the rate at which the gases are coming off. An apparatus resembling this has been described by Städel (Ber. **19**, 1,951).

Rubber connections must be avoided as far as possible, as bromine destroys them rapidly.

Flashes of flame and violent bursts of hydrobromic acid accompany the fall of each drop of bromine at first so that the

stream must be very slow. When the drops cease to produce instant effect, the mixture is allowed to cool a little and the remainder of the bromine is added. The retort is then heated on the water bath till the bromine disappears. More than 200 grams of the acid cannot well be worked up at once. The action under these conditions, which should not be departed from if it can be avoided, lasts from 3 to 5 hours.

When succinic anhydride is used the action is much quieter (cf. Sec. II. § 9).

To prepare bromosuccinic acid from the bromide, half a litre of water is taken for every 100 grams of succinic acid originally used. The water is heated to boiling, and, after the burner has been removed, the bromide is run in from a funnel provided with a stop-cock. The operation must be performed in a hood on account of the fumes given off. After all the bromide has been added, the liquid is filtered and the bromosuccinic acid is extracted with ether. The yield is 80–90 per cent. of the theoretical. To prepare the corresponding esters, the bromides are run into alcohol instead of water.

By this process the α -bromo-derivatives of the fatty acids may be prepared. The ingredients are taken so as to correspond with the equation—



Here the fluid fatty acid covers the amorphous phosphorus and the action is much less violent; still the necessary precautions must never be neglected. To obtain the bromo-acids themselves a larger amount of water is taken than for succinic acid, and the bromides are dropped into it while it boils. The bromo-derivative is then fractionated *in vacuo*. The yield is excellent.

The great advantage of the method as compared with the earlier ones, which nearly all required the use of sealed tubes, is that open vessels can be employed and yet the yields are very good.

According to Auwers and Bernhardt (Ber. **24**, 2,215), the general rule may be stated that in the aliphatic series as many bromine atoms are introduced as there are carboxyl groups in the molecule, provided that there is at least one α -hydrogen atom to be replaced.

When it is necessary for any reason to work with sealed tubes, the use of phosphorus is still advantageous. Thus Bujard and Hell (Ber. **22**, 68) found that while lepargylic acid heated for 8 hours at 100° with a molecular proportion of bromine was not acted upon at all, the addition of only $\frac{1}{10}$ per cent. of red phosphorus brought about the change completely in three hours.

Although a full statement of the case would lead us too much into detail, it ought to be mentioned that Krafft and Beddies (Ber. **25**, 488) found that heating fatty acids of large molecular weight directly with bromine in sealed tubes led to the formation of very curious and unexpected substitution products.

A variation in Volhard's process introduced by Alexander (Ann. **258**, 76) may be exemplified by mention of the case of phenylsuccinic acid. He placed the acid (10 gr.) in a retort with reflux arrangement, and poured over it phosphorus tribromide (11 gr.). No action took place, but when bromine (16 gr.) was dropped in slowly from a funnel the acid dissolved, hydrobromic acid gas was evolved with violence, and the bromide was produced. The product of the interaction was worked up in the way already described.

The author (Ann. **251**, 346) has found that Volhard's bromobromides are easily converted into dibromo-derivates by heating in a sealed tube to 100° with bromine.

3. Hydrobromic Acid.—Hydrobromic acid can be made in two ways. In Recoura's method (C. R. **110**, 784), the long known action of hydrogen sulphide on water and bromine is used. The gas is led into a tall vessel through a quantity of bromine, which is covered with a layer of water, or better still hydrobromic acid solution. After the water has become completely saturated, a regular evolution of hydrobromic acid begins. The gas is washed by passing through a solution of hydrobromic acid or potassium bromide to which some red phosphorus has been added. According to Fileti and Crosa (Gazz. Chim. **21**, 64), the gas is washed better by passage through a tower containing a mixture of asbestos and red phosphorus moistened with hydrobromic acid. By one of these means it is freed from bromine. It is not found to be contaminated with hydrogen sulphide, even when a rapid stream of this gas is used.

The other method we owe to Feit and Kubierschky (Ber. **25**, 411c). Potassium bromide (100 gr.) is dissolved in sulphuric acid of sp. gr. 1.41 (150 cc.), and the solution is distilled until the thermometer registers 200°. The well-nigh theoretical yield of hydrobromic acid is almost free from bromine, but contains a trace of sulphuric acid. Fractional distillation yields a portion boiling constantly at 126°. Its sp. gr. is 1.49, corresponding to 48 per cent. hydrobromic acid. From 150 grams of the bromide

about 200 grams of this acid are obtained. The gas is made from it by adding dry calcium bromide and warming.

When *alcohols are saturated with hydrobromic acid* and the solution is heated in sealed tubes at 100° , alkyl bromides are formed. If the acid is required in a perfectly dry condition, it is led first over phosphorus pentoxide. Usually, however, a bromine carrier, like phosphorus, is used in such cases.

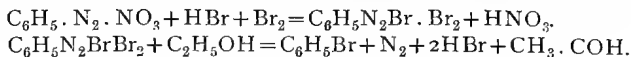
As an example of this method may be mentioned Veley's (Ch. News, **47**, 39) preparation of monobromhydrin. He saturated glycerol with dry hydrobromic acid, washed with caustic potash and distilled under diminished pressure.

The extraordinary solubility of hydrobromic acid in glacial acetic acid, amounting to 68 per cent. at ordinary temperatures (Ber. **11**, 1,221), renders such a solution very valuable in the preparation of *addition products*, and it is much used for this purpose. According to the directions of Anschütz and Kinnkutt, who prepared monobromohydrocinnamic acid from cinnamic acid, the substance may be placed with the solution in a sealed tube and heated if necessary in a water bath for a short time.

The temperature may, however, have some influence on the way in which the addition takes place. For instance, Kraut and Merling (Ann. **264**, 320) found that at 100° hydrobromic acid, used in the form of fuming hydrobromic acid, added itself to atropic acid so as to produce β -bromohydratropic acid, while, according to Fittig (Ann. **195**, 147), α -bromohydratropic acid is formed at 0° .

Similarly the process is influenced by other conditions. Thus dry hydrobromic acid and dry allyl bromide, $\text{CH}_2:\text{CH}.\text{CH}_2\text{Br}$, give chiefly trimethylene bromide, $\text{CH}_2\text{Br}.\text{CH}_2.\text{CH}_2\text{Br}$, while in presence of a solvent or with moist acid the production of propylene bromide, $\text{CH}_3.\text{CHBr}.\text{CH}_2\text{Br}$, is favoured. The latter statement has been called in question by Bogomolez (Ber. **11**, 1,257) however.

Bromo-derivatives are also obtained by the action of *hydrobromic acid on diazo-bodies* (Ann. **137**, 49), only in the case of this halogen acid the action is not so satisfactory as with hydriodic acid. The best way is to add strong hydrobromic acid and bromine water to the salt of the diazo-body. By this means a perbromide is produced, which, on boiling with alcohol, yields the bromo-derivative. The course of the action is represented by the equations—

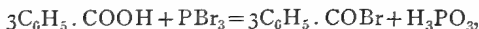


According to Richter (Ber. **8**, 1,428), this process frequently gives very poor results. Yet in his hands tribromoaniline gave a quantitative yield of tetrabromobenzene. He poured glacial acetic acid over the former, and led into it nitrous acid until the whole was dissolved. On adding concentrated hydrobromic acid, large quantities of crystalline diazotribromobenzene bromide, $C_6H_2Br_5N_2Br$, separated out. After boiling with an additional amount of acetic acid till nitrogen ceased to be evolved, tribromobenzene crystallised out. Jackson and Bancroft (Am. Ch.J. **12**, 289) state that when prepared in this manner it often contains some pentabromobenzene.

4. Phosphorus Pentabromide.—This substance cannot be used for making acid bromides, one respect in which it differs markedly from the pentachloride. Yet it can be used for making bromo-derivatives. Wurtz, for example, obtained ethylidene bromide (C. R. **47**, 418) with this reagent, and Gabriel (Ber. **24**, 3,100) speaks of effecting a bromination by its help.

Claus and Pollitz (J. pr. Ch. **149**, 41) succeeded in making α -bromoquinoline from carbostyryl by mixing one part of the latter with three parts of freshly prepared pentabromide, and heating the mixture for three to four hours at $120-130^\circ$. A constant stream of dry carbon dioxide was led through the apparatus, and the temperature was not allowed to exceed these limits, as otherwise there was a tendency to form more highly brominated products. The α -bromoquinoline was isolated by distillation in a current of steam. As the polybromo-derivatives come over last, the stream is interrupted before the drops of oil in the condenser begin to solidify.

Claisen states (Ber. **14**, 2,474) that phosphorus pentabromide has hardly any action on benzoic acid. The reaction takes place much more freely when *phosphorus tribromide* is used. Benzoic acid (3 mol.) is melted and powdered and mixed with the tribromide (2 mol.) and the whole heated in connection with a condenser. As the acid dissolves, an easily controllable reaction sets in during which streams of hydrobromic acid are evolved. After warming for forty-five minutes, the residue is distilled *in vacuo* and the distillate rectified at the ordinary pressure. The action follows the equation—



and 500 grams of the acid yields 400 grams of the bromide.

Phosphorus chlorobromide, PCl_3Br_2 , is often used in place of the pentabromide. Ladenburg and Friedel first showed that it had the same action on organic compounds containing oxygen as the latter. It is prepared by the action of bromine on excess of the trichloride at ordinary temperatures. The ingredients were placed by Michaelis (Ber. **5**, 9) in sealed tubes, the tubes being half filled with the materials. The reaction was complete in a few days, and the excess of the trichloride could be poured off the crystals of the chlorobromide. These were yellowish red in colour, and decomposed on heating to 35° .

By the help of this agent Paterno and Pisati (Ann. **221**, 137) converted aldehyde into ethylidene bromide, CH_3CHBr_2 , and Michael (Ber. **14**, 2,105) made butylidene bromide from butyl aldehyde.

5. Metallic Bromides.—*Calcium bromide* was used by Leilmann and Schwaderer (Ber. **22**, 1,327) for brominating piperidine. They mixed calcium hydroxide (300 gr.), suspended in water, with bromine (130 gr.) in a retort, and dropped a solution of piperidine in water into it, while a current of steam passed through the mixture. An oil, consisting of bromopiperidine, $\text{C}_5\text{H}_{10}\text{NBr}$, passed over.

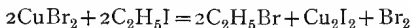
Some time before this Preibisch (J. pr. Ch. **116**, 316) had failed to observe any interaction between calcium bromide and nitromethane. Stenhouse, too (Ann. **91**, 309), had made bromopierin (tribromonitromethane) by the action of the same agent on picric acid. Bolas and Groves gave later (J. Ch. Soc. **23**, 153) the best proportions. Lime (4 parts) was slaked with water (50 parts), and to the cold mixture bromine (6 parts) and then picric acid (1 part) were added. On distilling, the bromopierin passes over with the first quarter of the distillate. It is dried with calcium chloride and purified by fractional distillation. The yield is about 95 per cent. of that theoretically derivable from their equation.

For the Sandmeyer reaction (see Sec. 11.) *cuprous bromide* solution is prepared as follows. Crystalline cupric sulphate (125 gr.) and potassium bromide (360 gr.) are dissolved in water (800 gr.), concentrated sulphuric acid (110 gr.) and copper (200 gr.) are added, and the whole is boiled, using a reflux condenser, till the colour has nearly vanished. Aniline, after being prepared for the operation, is converted by this agent into bromobenzene.

According to Gattermann (Ber. **23**, 1,218), finely divided copper may be employed as a carrier instead of the cuprous bromide. This action is described in detail under chlorination.

Cupric bromide, on account of its solubility in alcohol, is much used for converting organic iodides into bromides. For example,

by mixing its solution with ethyl iodide a change represented by the equation—



takes place, and the insoluble cuprous iodide is precipitated. In this case the bromine set free by the action might prove a disturbing element. Berthelot (Ann. **100**, 124) suggests the addition of finely divided copper to prevent interference with the course of the action from this source.

Potassium and silver bromides produce similar actions, but the yields are usually poor.

Worthy of mention is the discovery of Ciamician and Silber (Ber. **17**, 1,745) that a 5 per cent. solution of *potassium hypobromite* acts on pyrrol producing chiefly dibromomaleimide.

SECTION II.—CHLORO-DERIVATIVES.

The chlorination of organic compounds is brought about chiefly by the action of chlorine gas, phosphorus pentachloride, and hydrochloric acid. The following are less commonly employed: acetyl chloride, antimony trichloride, bleaching powder (hypochlorous acid), cuprous chloride, mercuric chloride, phosphorus oxychloride, phosphorus trichloride, sulphur monochloride and tetrachloride, sulphuryl chloride, chlorsulphonic acid, thionyl chloride.

1. Preparation of Chlorine.—Chlorine gas is prepared by covering a mixture of common salt (5 parts) and manganese dioxide (5 parts) with a cold mixture of concentrated sulphuric acid (12 parts) and water (6 parts), and then warming gently. These proportions give a regular stream of almost dry chlorine. Recently Klason (Ber. **23**, 330), has recommended the use of an earthenware apparatus charged with manganese dioxide and hydrochloric acid.

The use of bleaching powder as a source of chlorine in the laboratory was apparently first seriously suggested by Kämmerer (Ber. **9**, 1,548). The method became more popular after Winkler (Ber. **20**, 184) had devised a method of using it in an ordinary Kipp's apparatus, by moulding the powder into cubical pieces with the help of plaster of Paris. According to Klason (Ber. **23**, 330), the powder itself can be employed. Still the method has not preserved its popularity, as when the apparatus is used continuously many inconveniences arise.

Now that the "Badische Anilin und Sodafabrik" has introduced

liquid chlorine (Ann. **259**, 100) as an article of commerce, the larger laboratories will doubtless use it in this form.

As chlorine attacks corks and rubber stoppers, these should be coated with vaseline. Rubber stoppers which have been thoroughly rubbed with this substance are not only protected but even retain their softness for a considerable time.¹

2. The Use of Free Chlorine.—To bring about the *action of chlorine on liquids*, it may be led directly into them. To modify the violence of the action the liquid may be diluted with water, chloroform, acetic acid, or other suitable solvent. If this is undesirable then the chlorine itself may be diluted (Ann. **246**, 98), by forcing a stream of air or carbon dioxide through the generating apparatus, or by drawing such a stream through the apparatus with an aspirator.

The *amount of chlorine which has been taken up* is ascertained by weighing from time to time, and in this way, if the substance can take up several atoms of chlorine, the operation can be stopped when a sufficient amount has been introduced.

If an exact amount of chlorine is to be used, it is produced from weighed quantities of potassium permanganate or chlorate and hydrochloric acid, and a stream of carbon dioxide is finally conducted through the apparatus.

In the case of *aromatic bodies* the temperature has an important influence on the part of the molecule which the chlorine will attack. For example, Varnholt (J. pr. Ch. **144**, 22) finds that when phenol is treated with chlorine at a temperature just above that at which it would solidify, as much as 43 per cent. of *o*-chlorophenol is formed; while at the ordinary temperature a much smaller amount of this in proportion to the quantity of the para-compound is produced. For aromatic hydrocarbons, Beilstein and Geitner's rule (Ann. **139**, 332) holds. It is: that in the cold, in presence of chlorine carriers, the chlorine enters the phenyl group, while at the boiling-point of the substance the side chain is attacked. The latter action seems to take place with especial ease where the side chain is an aldehyde group, the

¹ In connection with this property of indiarubber, it may be mentioned that rubber stoppers absorb considerable quantities of hydrocarbons (Bunge, Ber. **23**, 113c.). In this connection also, attention may be drawn to Levoir's statement that the adhesion of rubber tubing to brass gas connections, when they have remained in contact for a considerable time, is due to the formation of crystallised sulphide of copper. It may be prevented by rubbing the tubing with soap. Grease should not be used.

acid chloride being formed. Benzoyl chloride was first made in this way. Liebig and Wöhler (Ann. **3**, 262) obtained it by passing chlorine into boiling benzaldehyde as long as hydrochloric acid was evolved, and rectifying the product. It seems to be made commercially in this way still.

Chlorine is always more active in sunlight than in diffused light. Thus chloroform can be converted into tetrachloride of carbon under those circumstances only.

When solids have to be chlorinated they are dissolved in water, acetic acid, chloroform, carbon tetrachloride, nitrobenzene, or ether, and these solutions are treated like liquids.

That a substance is saturated with the gas is recognised by its becoming green on account of the presence of free chlorine. The excess can be removed by adding some sulphurous acid, by warming, or by leading a rapid stream of air through the liquid. In the last case the completeness of its removal is tested by the action on potassium iodide and starch (Ber. **22**, 2525).

Agitation with mercury will also remove it, but in this case it must be noticed that when a liquid which has been so treated is shaken with ether, some chloride of mercury passes into the ether with the substance.

In the case of dissolved substances, the temperature and the solvent used have naturally an important influence on the product quite apart from considerations of isomerism. For example, the chlorination of *p*-acettoluide is very unsatisfactory at 0° and in acetic acid solution, and the yield is even poorer with other solvents. By splitting off the acetyl group, *m*-chloro-*p*-toluidine is finally formed (Ann. **168**, 196). But Erdmann (Ber. **24**, 2767) obtained this product quite easily by dissolving *p*-acettoluide (100 gr.) in hot glacial acetic acid (100 cc.), and passing chlorine through the solution. The gas was rapidly absorbed, and the liquid remained at the boiling-point without the application of external heat. From 1 kilogram of commercial *p*-acettoluide, 400 grams of *m*-chloro-toluidine, boiling within seven degrees, were obtained. Further Lellmann remarks (Ber. **24**, 4111) on this method that, in consequence of the high temperature, the product is less pure than need be, and that the yield can be raised from 38 per cent. to 42 per cent. by passing chlorine diluted with two volumes of carbon dioxide into a cold solution of *p*-acettoluide (50 gr.) in glacial acetic acid (400 gr.).

Sulphuric acid is used as a solvent in exceptional cases. Thus to

make tetrachlorophthalic acid, phthalic anhydride is warmed to 60° with sulphuric acid containing 50–60 per cent. of sulphuric anhydride (Ger. Pat. 50,177), a little iodine is added, and chlorine is passed in while the temperature is gradually raised to 180 – 200° . The tetrabromo- and tetraiodo-derivatives can be made in the same way.

Hafner (Ber. **22**, 2,525) tried in vain to chlorinate aniline and toluidine in the presence of large amounts of sulphuric acid of various strengths. But Claus and Philipson (J. pr. Ch. **151**, 59) succeeded in making dichloronaphthylamine by suspending β -naphthylamine sulphate in fifty times its weight of 80 per cent. sulphuric acid, cooling the mixture with ice, and leading into it chlorine gas in the proportion of two molecules of the latter to one of the substance. The chlorinated product was deposited when the mixture was poured into water. It was washed with ammonia to remove the acid, and recrystallised from alcohol or distilled in a current of steam.

Substances which can be melted without decomposition are fused, and chlorine is passed into the liquid mass. Thus *p*-nitrotoluene is melted in an oil bath, and the temperature gradually raised from 130° to 160° , while the calculated amount of chlorine is being led in. The resulting product is washed successively with water, dilute soda solution, and again with water, and is finally recrystallised from alcohol, yielding pure *p*-nitrobenzylidene chloride. Yet it should be mentioned that Zimmermann and Müller failed to obtain it in this way, and prepared it otherwise by the action of phosphorus pentachloride on *p*-nitrobenzaldehyde.

To secure the exposure of a large surface to the action of chlorine a device like that used by Cloëz (Bull. Ch. **39**, 636) may be employed. He dissolved citric acid in one and a half times its weight of water, and allowed this solution to drop on pieces of pumice in a vertical cylinder, while a stream of chlorine passed upwards to meet it. The product of the action was pentachloroacetone.

To render the action of chlorine as vigorous as possible, the substances on which it is to act may be brought in contact with it in the vaporous condition by boiling them in a flask attached to a reflux condenser and conducting the chlorine through a tube opening just above the surface of the liquid. Sometimes the vapour is mixed with chlorine and led through a red-hot tube containing animal charcoal, which has been previously ignited in an atmosphere of chlorine (Bull. Ch. **27**, 113). In this way phosgene gas is made from carbon monoxide and is caught in benzene, in which it dissolves very readily.

Whenever monochloroacetylene, which is spontaneously inflammable, is formed during chlorination, a rapid stream of an indifferent gas must be conducted through the vessels lest admixture of air should lead to explosions which might destroy the apparatus.

Chlorine Water. Perhaps the small solubility of chlorine in water has caused this reagent to be used less than it deserves to be. Witt (Ber. **8**, 143) states that, as might be expected, it acts much less energetically in this form than when used as a gas. It was used on this account by Körner in preparing dichloro-*p*-nitraniline. The nitraniline, which was converted into tar by chlorine gas, was dissolved in a large excess of hydrochloric acid, the mixture was cooled strongly, and chlorine water was added until the solution smelt strongly of chlorine. The product appeared in the form of a lemon-yellow precipitate. No tar was produced as long as the solution was kept cool.

Although, according to Gay Lussac,¹ the maximum absorption of chlorine by water takes place at 8°, when it takes up three volumes, yet by leading a rapid stream of the gas into water at 0° crystals of the composition, $\text{Cl} + 5\text{H}_2\text{O}$, are obtained, and this hydrate ought to be useful for work at low temperatures, especially where an excess of chlorine must be present throughout the operation.

This method was used by Stenhouse and Groves (Ann. **203**, 291), as it was found to be the only one by which tetrachlorobetorcinol, $\text{C}_8\text{H}_6\text{Cl}_4\text{O}_2$, could be obtained. They conducted a stream of chlorine through a mixture of ice and water, and then added a cooled solution of betorcinol in such quantity that the chlorine hydrate remained in slight excess. After 12–20 hours colourless crystals of the tetrachloro-derivative had separated out. Ditte (C. R. **95**, 1,283) employed the same method.

Grimaux (Ber. **5**, 222) used a solution of chlorine in chloroform, which takes up 28 per cent. at 0°, and 25 per cent. at 10°. By sealing up in a tube with benzene and with naphthalene he prepared benzene hexachloride and naphthalene tetrachloride, $\text{C}_{10}\text{H}_8\text{Cl}_4$, respectively.

Dilute *aqua regia* can also be used, but it leads often to the introduction of nitrogen as well as chlorine, and substances of complicated constitution may result.

When a calculated amount of *chlorine* is to be used *in a sealed tube*, Beilstein (Ann. **179**, 287) suggests the following method.

¹ Wurtz, "Dict. de Chimie," **1**, 858.

First fuming hydrochloric acid (25 cc.) is placed in the tube, a plug of glass wool is placed above it, and then the substance is added, and finally the calculated amount of potassium bichromate is put in. After the tube has been sealed the chlorine is evolved on heating.

3. Nascent Chlorine.—The application of nascent chlorine is a method which has long been in use. Thus Kolbe (Ann. **45**, 44) stated, in 1843, that thiophosgene, CSCl_2 , was best made by placing carbon disulphide, manganese dioxide, and hydrochloric acid in a closed vessel, and, with frequent agitation, allowing them to remain in contact for a considerable length of time. The method is now no longer used for making this particular substance however (Ann. **167**, 195).

Claus (Ber. **19**, 1,142) prepared dichloro-*a*-naphthochloroquinone, $\text{C}_{10}\text{H}_4\text{Cl}_4\text{O}_2$, by heating dichloro-*a*-naphthoquinone (10 gr.) with manganese dioxide (10 gr.) and pure hydrochloric acid, sp. gr. 1.2 (40 cc.), in sealed tubes for ten hours at 230° .

At present the usual method is to dissolve or suspend the substance in hydrochloric acid and add bichromate, or chlorate of potassium, or bleaching powder (*q.v.*). In this way Hofmann (Ann. **52**, 58) made chloranil from phenol. He advises that such operations should be carried out in basins, as the violence of the actions sometimes brings about explosions.

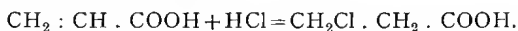
Fischer (Ber. **11**, 735) modified the process in making chloro-derivatives of naphthalene as follows. Using an idea of Depouilly's (Bull. Ch. 1865, **4**, 10), he mixed the naphthalene in a mortar with the amount of potassium chlorate necessary to chlorinate it to the desired extent, an operation demanding caution. The powder was then moistened with sufficient water to enable him to mould it into pellets, which he dropped one at a time into concentrated hydrochloric acid. Very little chlorine escaped, and by using one and a half times the amount of chlorate necessary to give four atoms of chlorine to each molecule of naphthalene he obtained naphthalene tetrachloride as the principal product.

4. Addition of Chlorine or Hydrochloric Acid to Unsaturated Compounds.—This method is of very wide application, and is often the only one by which the desired result can be attained. In gaseous form the substances unite readily, and it was in this way that Deimann and Trostwyk, in 1795, prepared the so-called "oil of Dutch chemists," ethylene chloride, by the union of ethylene

and chlorine. The usual method is to dissolve the unsaturated body in water, acetic acid, ether, or other solvent, and add a solution of chlorine or hydrochloric acid in the same medium.

The presence of sufficient chlorine may be tested by the fact that the mixture should have no, or at least hardly any, power to decolourise dilute bromine water.

An example of the use of the addition method is supplied by the β -derivatives of the fatty acids. The union of chlorine with the carbon atom not already combined with carboxyl can be achieved by adding hydrochloric acid to the unsaturated compound. Thus β -chloropropionic acid is made by the addition of hydrochloric acid to acrylic acid (Ann. **163**, 96).



Chlorine derivatives of terpenes are likewise made by the addition of hydrochloric acid. Thus Deville (Ann. **71**, 348), in 1843, found that terpene unites with that acid to form the compound $\text{C}_{10}\text{H}_{18}\text{Cl}_2$, and Wallach (Ann. **236**, 9) has recently stated that limonene in acetic acid solution unites with the same acid to form the body, $\text{C}_{10}\text{H}_{16} . 2\text{HCl}$, which is deposited at once, and the same is true of hydrobromic and hydriodic acids.

5. Action of Hydrochloric Acid on Alcohols.—The general action corresponds to the equation, $\text{CH}_3\text{OH} + \text{HCl} = \text{CH}_3\text{Cl} + \text{H}_2\text{O}$, and chloro-derivatives of the hydrocarbons are formed.

The hydrochloric acid may be prepared (Hofmann, Ber. **1**, 272) by filling a flask to the extent of one third with commercial hydrochloric acid, and allowing concentrated sulphuric acid (sp. gr. 1.843) to flow in from a funnel provided with a stop-cock. After some preliminary irregularity, during which the possible passage of the substance to be acted upon back into the flask must be guarded against, the evolution of the gas becomes very regular and continues till the sulphuric acid has attained a density of 1.566 and only 0.32 per cent. of hydrochloric acid remains behind. Another method is to place large pieces of ammonium chloride in a flask and drop concentrated sulphuric acid upon them from a funnel. Biltz (Z. physik. Ch. **2**, 965) contends that Kipp's apparatus gives better results, but the use of salammoniac and sulphuric acid in this way is dangerous because when the apparatus is shaken the hydrochloric acid gas dissolved by the acid is apt to be suddenly evolved, and, by the pressure thus created, to project the acid through the upper opening in the apparatus with considerable violence.

The use of hydrochloric acid may be illustrated by Geuther's method of preparing ethyl chloride (Z. Ch. **1871**, 147). Hydrochloric acid is passed into alcohol, and the solution is then heated slowly on the water bath, while the gaseous ethyl chloride is washed in water at 20° and dried with chloride of calcium. The best yield is obtained from alcohol diluted with two volumes of water and nearly saturated with the gas.

The addition of water to alcohols is rendered necessary by the fact that they are unable by themselves to dissolve sufficient hydrochloric acid. Thus Malbot (Bull. Ch. [3], **1**, 604) found that although in saturating amyl alcohol with hydrochloric acid the volume increased from 1 litre to 1.7 litres, this amount did not suffice for its conversion into amyl chloride. Half as much again, by volume, of concentrated hydrochloric acid had to be added. By heating this mixture at 120–130° pure amyl chloride, boiling at 97°, and free from the alcohol was obtained. If the temperature is allowed to reach 150°, by-products are formed.

To Groves (Ann. **174**, 372) we owe the use of zinc chloride (cf. Chap. XII. § 36) in this reaction. He uses 1 part of fused zinc chloride to 1.5–2 parts of the alcohol, and boils the mixture with a reflux arrangement while hydrochloric acid is being led into it. At first the gas is absorbed, but soon a stream of (*e.g.*) ethyl chloride issues from the condenser at a speed corresponding to that at which the acid is supplied. Krüger (J. pr. Ch. **122**, 195) likewise recommends the method, while Schorlemmer (Ber. **7**, 1,792) states that the only objection to it is that, when primary alcohols of high molecular weight are treated, the zinc chloride causes water to be split off, leaving unsaturated hydrocarbons of the ethylene series, which, with hydrochloric acid, yield secondary chlorides.

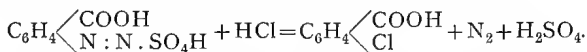
The hydroxyl groups of bodies belonging to other classes may also be replaced by chlorine in this way. Thus glycollic acid gives monochloroacetic acid, and Werigo and Melikoff (Ber. **12**, 178) obtained a chlorolactic acid and dichloropropionic acid by heating glyceric acid, $\text{CH}_2\text{OH} \cdot \text{CHOH} \cdot \text{COOH}$, for some time in a sealed tube with hydrochloric acid saturated at 0°.

6. Halogen Compounds from Diazo-Bodies and Hydrazine Derivatives.—The action of haloid acids on the sulphates of diazo-bodies whereby halogen derivatives are formed is a very important one.

The sulphates are easily prepared from the nitrates by dissolving

in a mixture of equal parts of sulphuric acid and water and adding first alcohol and then ether to the solution. The sulphate soon comes out in crystalline form.

The reaction in the case of the sulphate of diazobenzoic acid, for example, takes place in accordance with the equation—



Griess (Ber. **18**, 960) recommends the use of 3-5 parts of haloid acid for each part of the diazo-body. The reaction is completed by boiling and the product crystallises out. In the above case it consists of nearly pure chlorobenzoic acid.

The researches of Baeyer and of Zincke have shown that primary aromatic hydrazines are easily converted into the corresponding hydrocarbons by oxidation. And when the hydrochloric acid salts are employed almost theoretical yields of the chloro-derivatives of the same hydrocarbons are obtained.

The operation, according to Gattermann and Hölzle (Ber. **25**, 1,075) is carried out as follows: A solution of cupric sulphate (100 gr.) in water (100 cc.) is heated to boiling in a flask of 1.5 litres capacity, provided with dropping funnel and a reflux condenser. A hot solution of phenylhydrazine (10 gr.) in concentrated hydrochloric acid (25 cc.) and water (100 cc.) is run in. Nitrogen is evolved with violence, metallic copper is deposited, and an oil passes over with steam which, on rectification, yields chlorobenzene, boiling at 132°. The amount represents 86.4 per cent. of the theoretical yield.

Wallach and Kölliker (Ber. **17**, 396) state that when pure amidoazobenzene hydrochloride (10 parts) is boiled, with reflux arrangement, with hydrochloric acid of sp. gr. 1.12 (100 parts) the compound is decomposed in a few hours, and a current of steam carries over trichloroquinol. The yield is poor however.

Losanitsch (Ber. **18**, 39) describes a method of replacing amido-groups in aromatic bodies by halogens, without an intermediate diazo-stage, by acting with a mixture of the halogen acid and nitric acid. The results do not seem however to commend the method strongly.

7. Replacement of Bromine and Iodine by Chlorine.—By shaking bromo- and iodo-derivatives with silver chloride they exchange halogens, and bromide or iodide of silver is formed. Thus, according to Conrad and Eckhardt (Ber. **22**, 74), γ -hydroxyquinol-

dine methiodide yields the corresponding chloride in crystalline form by digesting a warm solution of the former in water with the necessary amount of freshly precipitated silver chloride and evaporating the filtered liquid.

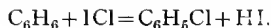
Gaseous chlorine has likewise the power of driving out other halogens. Thus tetrachlorothiophene was made by Weitz (Ber. **17**, 795) passing a rapid stream of chlorine through dibromothiophene till the bromine was removed. During this operation the vessel was cooled with ice. Then the resulting substance was boiled for some time with alcoholic potash to decompose addition products. Finally pure C_4Cl_4S was obtained by fractionation.

When organic acids are in question it is best to use the silver salts and to suspend them in ether (J. pr. Ch. **140**, 111), or chloroform, in order to obtain the chloro-acids. With the dry salts complicated products result, as might be expected. Thus Krutwig (Ber. **15**, 1,340) states that silver acetate yields chloroacetyl chloride, and according to Nef (Ber. **25**, 842) the dry silver salt of chloranilic acid gives tetrachlorotetraketohexamethylene.

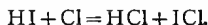
Frequently chlorine, and the same remark applies to bromine (cf. p. 169), acts only on salts of compounds and not on the compounds themselves. Thus chloronitromethane, CH_2NO_2Cl , can be obtained only by the action of chlorine on sodio- or potassio-nitromethane (Ber. **8**, 608).

8. Chlorine Carriers.—While chlorine can only act by substitution on saturated fatty substances, in the aromatic series the action takes the form of an addition, on account of the presence of the double bonds. Thus benzene gives benzene hexachloride. The difference can be recognised by the fact that during substitution hydrochloric acid is necessarily evolved, while in the case of addition no such evolution is observable.

Müller (Z. Ch. **1862**, 100) found, however, that when he tried to make iodo-derivatives in the aromatic series by the use of *iodine chloride* a violent action took place, and nothing but chloro-derivatives were obtained. This led him to make the same experiment with benzene, and he found that, as a matter of fact, when a little iodine was added and chlorine was passed into the liquid, a regular evolution of hydrochloric acid gas occurred. This action takes place in consequence of the formation of iodine chloride, which leads to the formation of hydriodic acid according to the equation—



The chlorine acts on this further, reproducing iodine chloride—



The only disadvantage attending the use of iodine as a chlorine carrier is the fact that small quantities of iodo-derivatives are formed.

Even earlier than this the chlorinating power of *antimony trichloride* had been noticed by Wöhler, and Hofmann (Ann. **115**, 266) had made carbon tetrachloride by adding it to chloroform and passing in chlorine. It seems not to have been applied to aromatic compounds at that time.

Molybdenum pentachloride was found by Lothar Meyer (Ber. **8**, 1,400), when he tried to recrystallise it from benzene, to attack the latter with evolution of hydrochloric acid. He suggested therefore that it might be used instead of iodine as a chlorine carrier.

Aronheim's experiments confirmed this supposition. Benzene, containing about one per cent. of molybdenum pentachloride, was found to absorb chlorine with such avidity that hardly a trace of it could be discovered mixed with the hydrochloric acid gas which poured off in torrents. Carbon disulphide (Ber. **9**, 1,788) is likewise powerfully attacked by chlorine in presence of this agent.

The difficulty in preparing the molybdenum pentachloride (Ann. **169**, 344) led to a search for other metallic chlorides which should have the same effect. Page's researches (Ann. **225**, 199) showed that molybdenum trichloride, ferric chloride, aluminium trichloride, thalious chloride (TiCl) and thallic chloride (TiCl_3), were also serviceable as chlorine carriers.

Ferric chloride and the chlorides of thallium are specially valuable. In their presence the chlorination advances rapidly and with regularity. The advantage lies on the whole with the latter, as they are easy to separate from the products of the action, while ferric chloride produces by-products which often leave appreciable residues.

For example, to nitrobenzene (75 gr.), which is not attacked by chlorine, dry ferric chloride (9.56 gr.) was added, and a slow stream of chlorine was passed into the mixture at 100° . The weight increased by 82.57 gr., and tetrachloronitrobenzene was found to be the chief product. At a higher temperature, hexachlorobenzene was formed. It was washed with water and recrystallised from carbon disulphide.

In general only two per cent. of ferric chloride requires to be added.

Antimony trichloride was used by Beilstein and Kurbatow (Ann. **182**, 102) as follows: For example, nitrobenzene (200 gr.) was warmed with the trichloride (40 gr.), and a rapid stream of chlorine was passed through the mixture. When the flask and material had gained 68 grams in weight, the contents were washed successively with hydrochloric acid, water, caustic soda, and water again. The result was distilled, and the fraction boiling between 230° and 245° was cooled strongly. Crystals of *m*-chloronitrobenzene were deposited.

The following process is used on a large scale (Ger. Pat. 32, 504): Phthalic anhydride (5 parts) and antimony pentachloride (30 parts) are heated for several hours at 200° . The heating is then continued for eight to twelve hours, during which a current of chlorine gas is conducted into the fused mass. By this means almost the whole of the anhydride is converted into the tetrachloro-derivative. The antimony pentachloride, which may contain some of the trichloride, is first distilled off and preserved for use in other similar operations. Then, on further heating, the tetrachlorophthalic anhydride comes over.

The metals in the form of powder may be used instead of their chlorides, the transformation into the latter being effected by the chlorine itself.

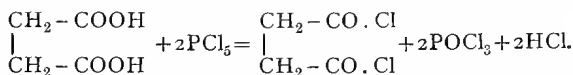
Willgerodt (J. pr. Ch. **143**, 391) finds that the halogen carrying power of the elements is a function of their atomic weights.

Willgerodt and Salzman (J. pr. Ch. **147**, 465) chlorinated *p*-bromotoluene in presence of *metallic iron*. Soon after the action starts, a considerable elevation of temperature takes place, under whose influence the substance melts. A little later artificial cooling has to be resorted to. As soon as the proper increase in weight shows that the operation is completed, the product, which is brown in colour from the presence of iron compounds, is shaken with caustic soda and with water. On fractionating the dried and now colourless liquid, the greater part passes over between 210° and 220° . It is a mixture of the two theoretically possible monochloro-*p*-bromotoluenes.

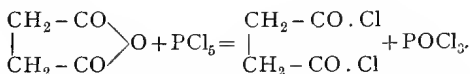
Petricou (Bull. Ch. [**3**], **3**, 189) added granulated *tin* (90 gr.) to benzene (400 cc.), and passed a current of chlorine through the liquid while it was boiling with reflux arrangement. In thirty-six hours, dichlorobenzene was formed, and in eighty-six hours, tetrachlorobenzene. In this case, however, the ease with which the chloride of the metal could be removed from the product would

scarcely compensate for the excessive amount of time consumed by the process.

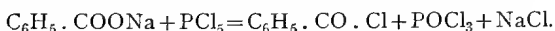
9. Phosphorus Pentachloride.—This is an agent in very general use for replacing hydroxyl groups by chlorine. It was used by Dumas and Peligot (1836) for the production of cetyl chloride from cetyl alcohol, and ten years later Cahours (C. R. **22**, 846, and **25**, 724) examined thoroughly both the substance itself and its action on cinnamic acid, benzaldehyde, and other bodies. It is used particularly for the conversion of acids into acid chlorides. In the case of succinic acid, for example, the following action takes place :



If acid anhydrides are used, only half as much of the pentachloride is necessary—



Instead of the acids, the salts of the alkali metals may be taken, a method which is valuable where the free acids can only be obtained perfectly dry with difficulty—



The operation is always carried out in practice by adding phosphorus pentachloride gradually to the dry acid. If the action is very violent, the vessel may be cooled during the action, and the acid and chloride may be cooled before mixing. The vessels used are flasks or retorts in connection with reflux condensers. The following will serve as illustrations.

The action on hydroxyazo-compounds was found by Paganini (Ber. **24**, 365) to be characteristic. By heating equi-molecular quantities of *p*-tolueneazophenol and pentachloride of phosphorus on the water bath for two hours, an orange-red mass was obtained, which was freed from excess of the chloride by treatment with water. Alcohol extracted from the product *p*-tolueneazochlorobenzene, $\text{CH}_3 \cdot \text{C}_6\text{H}_4 \cdot \text{N}_2 \cdot \text{C}_6\text{H}_4\text{Cl}$, and the residue, recrystallised from acetone, yielded *p*-tolueneazophenyl phosphate, $(\text{CH}_3\text{C}_6\text{H}_4\text{N}_2\text{C}_6\text{H}_4\text{O})_3\text{PO}$.

By way of *dilution* to restrain the action of the pentachloride, it may be mixed with five times its weight of phosphorus oxychloride.

Benzene, chloroform, or petroleum ether may be used for the same purpose. For example, Baeyer (Ber. **12**, 456) heated isatin (5 gr.) with phosphorus pentachloride (7 gr.) in dry *benzene* (8–10 gr.) in a flask, connected with a reflux condenser. When the violence of the action had abated, the mass solidified to a cake of brown crystals of isatin chloride, C_8H_4ClNO . The yield was 4 grams in place of the theoretical 5.5 grams.

Geigy and Königs (Ber. **18**, 2,402) dissolved *o*-nitrobenzyl alcohol just as in making the chlorides of cinchona alkaloids, in dry *chloroform* (10 parts), cooled the solution, added the calculated amount of pentachloride, and afterwards decomposed the resulting oxychloride with water. On separating the chloroform layer and distilling off the solvent, *o*-nitrobenzyl chloride remained.

A modification of this method is recorded by Berkenheim (Ber. **25**, 686), who covered an amount of the pentachloride, slightly in excess of that necessary, with *petroleum ether*, and added menthol (100 gr.) in small portions to the carefully cooled mixture. He waited after each addition until the evolution of hydrochloric acid gas had ceased. The petroleum ether was removed and the product distilled, when 15 gr. of a fraction boiling at 167–169° and 70 gr. of another boiling at 209–210° were obtained. The former was menthene, $C_{10}H_{18}$, and the second, menthyl chloride, $C_{10}H_{19}Cl$. The first had arisen as the result of the abstraction of water from the menthol, $C_{10}H_{19}OH$.

Wallach (Ann. **263**, 148) dissolved fenchyl alcohol (45 gr.) in petroleum ether of low boiling-point (80 gr.), and added slowly to the solution phosphorus pentachloride (60 gr.). A violent action took place, at the conclusion of which the liquid was poured off from a small quantity of unchanged pentachloride, and the petroleum ether and oxychloride were distilled off *in vacuo* by heating on the water bath. The fenchyl chloride, being liquid, could not be purified by recrystallisation, and was therefore driven over with steam to free it completely from phosphorus compounds. Perfect purity was finally attained by fractionation *in vacuo*.

Pechmann (Ann. **264** 282) moistened crude cumalinic acid (14 gr.) with phosphorus oxychloride in a fractionating flask connected hermetically with a receiver, and added phosphorus pentachloride (22 gr.) in small portions, assisting the action meanwhile by heating on a water bath. When the change was complete the oxychloride was distilled off on an oil bath, and the residue distilled under a pressure of 80 mm. It all passed over at about 180°. He did not succeed however in freeing the chloride entirely from phosphorus.

The separation of the products of actions like the above, chiefly acid chloride and phosphorus oxychloride, is sometimes attended with difficulty.

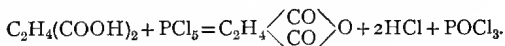
If excess of pentachloride has been used a little phosphorus is added so as to form the trichloride, which is a liquid boiling at 74° and is easily distilled off.

When the acid chloride is volatile without decomposition, it may be separated from the oxychloride by fractional distillation either under atmospheric pressure, or if necessary under diminished pressure.

It is stated by Krafft and Bürger (Ber. **17**, 1,378) that the higher homologues of acetic acid, when mixed with pentachloride in molecular proportions, warmed on the water bath, and finally heated to 150° under 15 mm. pressure to remove the oxychloride, give as residue the exact theoretical amounts of the chlorides, $C_nH_{2n-1}OCl$. They prepared thus chemically pure lauryl chloride, $C_{12}H_{23}OCl$, myristyl chloride, $C_{14}H_{27}OCl$, and other members of the series.

Gräbe and Bungener (Ber. **12**, 1,079) found that in preparing the chloride of phenylacetic acid, although the action seemed to proceed normally, a yield of only 10 per cent. was obtained on distilling. When they repeated the operation by heating equimolecular parts of the substances, instead of distilling the product they heated it to $100-120^{\circ}$, and passed through it a stream of dry carbonic acid until nothing further passed over. The almost colourless residue in the retort consisted of the chloride in relatively large quantity and almost pure.

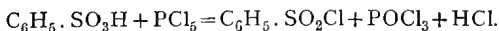
A residue obtained in this way is apt to contain some acid anhydride formed according to the equation—



It may be dissolved out with a little absolute ether.

The separation may be effected in quite another way by adding dry petroleum ether to the mixture, as long as the cloudiness increases, and shaking. The petroleum ether mixes easily with the oxychloride (Ber. **8**, 301), while the acid chloride settles to the bottom when the mixture is left at rest.

Sulphonic Acids are converted into their respective chlorides by means of phosphorus pentachloride, in accordance with the equation—

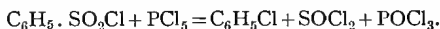


The chlorination is carried out just as in the case of carboxyl acids, only here exceptional actions occasionally occur. Thus Claus and Knyrim (Ber. **18**, 2926) failed to obtain the chloride of α -naphthol- β -sulphonic acid by using the pentachloride with the sodium salt of the acid in equimolecular proportions. Part of the acid always remained unchanged and part was converted into dichloronaphthol. Similar irregularity is shown by β -naphthol- α -sulphonic acid (Ber. **18**, 3,157). On the other hand, Zielstorff (Dissert. Greifswald, 1890) prepared the chloride of diphenyldisulphonic acid by drying its potassium salt at 180° , and warming it with two molecules of pentachloride. After washing the product with water until it was neutral, it was purified by recrystallisation from chloroform.

Such chlorides can also be recrystallised from ether, benzene, acetic acid, carbon disulphide (Ber. **24** 654c), and other solvents. Thus Jäkel (Ber. **19**, 189) obtained thiophenedisulphonic chloride, $C_4SH_2(SO_2Cl)_2$, from ether in needles.

The sulphonic chlorides are distinguished from the ordinary acid chlorides by the fact that they are often very stable towards water, and prolonged boiling with this, or even with dilute alkalis, may be necessary to convert them into the corresponding acids.

Barbaglia and Kekulé (Ber. **5**, 876) state that sulphonic chlorides are decomposed by phosphorus pentachloride at 200° , in accordance with the equation—

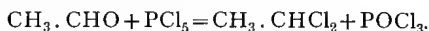


The formation of these products has been explained by Michaelis (Ber. **5**, 929) in a different manner.

Using this action, Königs and Geigy (Ber. **17**, 1,832) obtained some, till then unknown, chlorinated derivatives. Thus they heated the barium salt of pyridinesulphonic acid with pentachloride to 200° , poured the product into ice-cold water, and, after the chlorine compounds of phosphorus had been decomposed, distilled the product in a current of steam. From the distillate a dichloropyridine and a trichloropyridine were isolated.

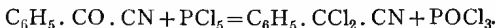
Erdmann (Ber. **20**, 3,185) used the same process with naphthylamine-sulphonic acid.

In *aldehydes and ketones*, phosphorus pentachloride replaces the carbonyl oxygen by Cl_2 , thus :

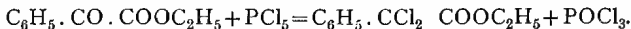


It acts energetically on acid cyanides. Thus Claisen (Ber. **12**, 626) states that with benzoyl cyanide it gives a yellow liquid, which,

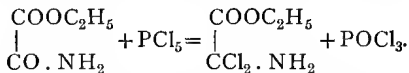
on being poured onto ice, leaves a heavy oil. When this is washed with caustic potash to remove any remaining cyanide and rectified, it consists of pure phenyldichloroacetonitrile—



With the ester of phenylglyoxylic acid it forms phenyldichloroacetic ether which can be purified by fractionation—



Wallach (Ber. **8**, 301) announced the fact that when an acid amide contains more than one carbonyl group, the oxygen attached to the same carbon atom with the amido-group is first attacked. Thus the ethyl ester of oxamic acid gives dichloroamidoacetic ether—



From 50 grams of oxamic ether, 50 grams of the chloro-product were finally obtained by precipitation with petroleum ether.

This reaction was of some importance in connection with the synthesis of indigo. When the attempt was made to reduce isatin,

$\text{C}_6\text{H}_4 \begin{array}{l} \diagup \text{CO} \cdot \text{CO} \\ \diagdown \text{NH} \end{array}$ (pseudoisatin), only the carbonyl group next to the benzene ring is attacked. But Baeyer (Ber. **11**, 1,296), by first treating it with phosphorus pentachloride and then reducing, succeeded in removing the oxygen from the other carbon atom also. The lactime chloride was probably formed as an intermediate product, $\text{C}_6\text{H}_4 \begin{array}{l} \diagup \text{CO} \cdot \text{CCl} \\ \diagdown \text{N} \end{array}$.

Homologues of benzene can be chlorinated by means of the pentachloride. According to Colson and Gautier (C. R. **102**, 690), the substances are placed in sealed tubes and heated at 200°. They prepared hexachloroxylene, $\text{C}_6\text{H}_4(\text{CCl}_3)_2$, for example, in this manner. The chlorine does not appear in the ring until the hydrogen atoms of the side chains have been fully replaced.

10. Acetyl Chloride.—In view of the fact that acetyl chloride is frequently employed for introducing an acetyl group, it may be worth mentioning that its use seems sometimes to lead to chlorination. At all events Becker (Ber. **20**, 2,007) states that, on heating acetyl chloride and azobenzene in a sealed tube at 160° for four

hours, he obtained chiefly *p*-chloroacetanilid and *p*-dichloroazobenzene.

Bredt (Ann. **256**, 334) found that when levulinic acid was mixed with acetyl chloride (2 mol.) a violent action ensued which had to be restrained by external cooling. After the excess of acetyl chloride and the acetic acid had been removed by distillation *in vacuo*, the residue was found to consist of levulinic chloride, which passed over at 80° under a pressure of 15 mm.

11. Antimony Pentachloride.—This substance, which has already been noticed as a chlorine carrier, is used also for direct chlorination. Thus Beilstein (Ann. **179**, 284) heated *p*-chlorobenzoic acid (1 part) with antimony pentachloride (7.5 parts) at 200° for several hours. Dichlorobenzoic acid was obtained from the product by first removing the antimony with concentrated hydrochloric acid, then dissolving the residue in ammonia, evaporating to dryness, and finally re-acidifying.

Merz and Weith (Ber. **16**, 2,870) used the pentachloride for perchlorination; that is to say, for the addition of chlorine until all the double bonds of the substance had been converted into single ones. The material under investigation was usually treated with a large excess of the antimony compound in a sealed tube at 350°, and the heating continued till no further production of hydrochloric acid could be noticed. If the action of the chloride was too violent at first, a preliminary treatment with chlorine gas preceded the enclosure in the tube. Phenanthrenequinone gave perchlorodiphenyl, C₁₂Cl₁₀, dibenzyl gave perchlorobenzene and perchloroethane, and β-naphthonitrile gave perchlorobenzene.

Following the same line of work, Hartmann (Ber. **24**, 1,025) has shown that many substances of the fatty series, such as hydrocarbons, palmitic acid, and wax, on being treated with antimony pentachloride at 300–450° in presence of a little iodine, are converted into perchloromethane and perchlorobenzene. These substances may, in fact, be regarded as the ultimate combustion products, so to speak, of aliphatic derivatives in respect to chlorine.

Henry states (C. R. **97**, 1,491) that antimony pentachloride can likewise be used for exchanging bromine for chlorine. Thus by heating chloroethylene bromide, CH₂Br–CHClBr, with it, bromoethylidene chloride is produced, and in like manner (Ann. Ch. Ph. **30** 271) dibromomethane gives dichloromethane.

12. Bleaching Powder and Hypochlorous Acid.—Bleaching powder is used both alone and in presence of acids as a chlorinating agent. For example, Beilstein (Ann. **179**, 286) found that when

o-chlorobenzoic acid was gently boiled with bleaching powder solution, dichlorobenzoic acid was easily formed, although it was difficult to avoid the simultaneous formation of the trichloro-derivative.

Witt gives the following method of preparing chlorine derivatives of aniline: Acetanilide (5 parts) is dissolved in a warm mixture of glacial acetic acid (10 parts) and alcohol (10 parts); the mixture is diluted with water (100 parts), and, the solution having been brought to 50°, a bleaching powder solution (100 parts), containing 10 per cent. of calcium hypochlorite, is added slowly during continuous agitation. A snow-white precipitate, consisting of minute needles of monochloroacetanilide soon appears. It is purified by recrystallising from warm acetic acid or alcohol (cf. Bender, Ber. **19**, 2,272).

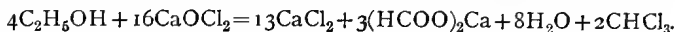
By altering the conditions slightly a different result is obtained. The acetanilide (5 parts) is dissolved in a boiling mixture of acetic acid (20 parts) and water (100 parts), and, the flame having been removed, bleaching powder solution of the above concentration (400 parts) is slowly added. The first 100 parts produce a precipitate which, after 200 parts have been added, is transformed into the much more compactly crystalline dichloroacetanilide. If the solution is once more warmed, in case its temperature has fallen below 60–70°, and the remainder of the bleaching powder added a little at a time and with constant agitation, a heavy oil sinks to the bottom of the vessel. It consists of an addition product of hypochlorous acid and dichloroacetanilide. If the oil is taken up with ether and the extract dried with calcium chloride, it deposits on standing beautiful crystals of the dichloroacetanilide as the result of gradual decomposition. This substance may be obtained more readily by interrupting the addition of bleaching powder as soon as the mass has become yellow and acquired a pulpy consistency.

Tscherniak (Ber. **9**, 146) added ethylamine hydrochloride (25 gr.) to bleaching powder (250 gr.) which had been mixed with water so as to form a paste in a large flask, and distilled the mixture as long as drops of oil passed over. The distillate was then treated once more in the same manner with an equal amount of bleaching powder and redistilled. The second distillate was treated successively with sulphuric acid, caustic soda, and water, and was finally dried and fractionated. A good yield of a dichloroethylamine was obtained, to which he ascribed the constitution $\text{CH}_3 \cdot \text{CH}_2 \cdot \text{NCl}_2$ (?).

Chandonon (Ber. **16**, 1,749) states that alkaline hypochlorites act on phenols in dilute (3 per cent.) solutions at the ordinary tem-

perature, and that by using the calculated amounts of the material the operation may be carried as far as the production of trichloro-derivatives. Thus when a mixture containing phenol and sodium hypochlorite (made from bleaching powder and soda) is neutralised with hydrochloric acid, *o*-chlorophenol separates out as an oil. The yield is considerable.

It is thus evident that bleaching powder is a valuable chlorinating agent, although it is usually hard to predict what its exact action will be in any given case. Liebig (Ann. **1**, 199) observed that it converted alcohol and acetone into chloroform. Then Belohoubek (Ann. **165**, 350) showed that while this statement was true for ethyl alcohol, it did not hold for methyl alcohol. Finally Goldberg (J. pr. Ch. **132**, 114) made an exhaustive examination of the action of bleaching powder on various alcohols, and proved that chlorine never entered the carbinol group; that, in fact, this part of the molecule was always oxidised to formic acid or carbonic acid. According to Goldberg the following equation best represents the amount of chloroform obtained when working on a manufacturing scale, the actual result being uniformly less favourable however:



Chlorination can be accomplished with bleaching powder in presence of nascent hydrochloric acid, but the employment of potassium chlorate is usually to be preferred.

The action of *hypochlorous acid* on organic bodies can be best studied in connection with that of bleaching powder.

Now that its power in breaking ring structures (cf. *e.g.* Ber. **25**, 1,493) has come to be recognised, it must be regarded as a valuable reagent for such purposes.

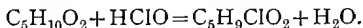
It may be well first to describe the best ways of *preparing hypochlorous acid*. Reformatzky (J. pr. Ch. **148**, 396) gives the following method: The chlorine is evolved from a mixture of hydrochloric acid and potassium bichromate contained in a flask of $1\frac{1}{2}$ litres capacity. The gas, after being washed by passing through water contained in a three-necked bottle, is led into a flask of about 500 cc. capacity, containing mercuric oxide covered with five times its volume of water. This flask stands in water cooled with ice, and is provided with a doubly bored stopper. The tube leading the chlorine passes through one hole and reaches almost to the bottom of the flask, while from the other projects a second tube which conducts any escaping gases into the chimney of the hood. Towards the conclusion of the action, which is marked by the disappearance of the oxide of mercury, the flask is

agitated periodically. The solution of hypochlorous acid and mercuric chloride in water which remains is now distilled to separate the former from the latter, and the receiver is connected with the chimney of the hood as before. Large quantities of hypochlorous acid are easily prepared in this way. As a part of the acid is decomposed, yielding free chlorine during the distillation, and this may have a disturbing effect in some actions, producing, for example, by-products where addition to unsaturated bodies is in question, it is advisable to remove it by passing a stream of carbon dioxide through the solution until all odour of chlorine is removed.

Another method is the well-known one of adding a sufficient amount of boric acid to a bleaching powder solution. This gives a preparation, however, containing a large quantity of foreign material.

The use of hypochlorous acid may be illustrated by an experiment of Reformatzky's (J. pr. Ch. **148**, 400). He placed allyldimethylcarbinol (20 gr.) in a large flask with some ice-cold water, and added a solution of hypochlorous acid, free from chlorine, in small portions until the odour of the acid became permanent. The slight excess was then destroyed by means of sodium thiosulphate. On extracting the filtrate with ether and evaporating, 23 grams of the monochlorhydrin of glycerol remained, while a yield of 30 grams was theoretically possible.

Schlebusch (Ann. **141**, 323) mixed equivalent quantities of sodium valerate and hypochlorous acid in water solution. After standing for several days in the dark, the solution deposited monochlorovaleric acid along with unchanged valeric acid—



Carius (Ann. **140**, 317) found that hypochlorous acid was capable of adding itself to all unsaturated organic bodies, one molecule of HClO being taken up for every H_2 that was lacking to complete saturation.

Schützenberger (C. R. **52** 135) is responsible for the discovery that, when anhydrous hypochlorous acid acts on acetic anhydride at a low temperature, a liquid of the same composition as monochloroacetic acid, but differing widely from it in properties, is formed. He named it chlorine acetate.

13. Cuprous Chloride, Sandmeyer's and Gattermann's Reactions.—The use of cuprous chloride for the replacement of the amido-group in aromatic compounds by chlorine was introduced by Sandmeyer (Ber. **17**, 1,633). He discovered that large

quantities of chlorobenzene were formed by the action of cuproacetylene on diazobenzene chloride, and attributed this to the influence of cuprous chloride formed during the action. Further experiments showed that this view was correct.

The preparation of chlorobenzene, according to his method, is as follows: Aniline (30 gr.) is dissolved in hydrochloric acid of sp. gr. 1.17 (67 gr.) diluted with water (200 cc.). To the cooled solution sodium nitrite (23 gr.) dissolved in water (60 cc.) is gradually added. This mixture is now allowed to flow, drop by drop, through a funnel provided with a stop-cock, to a 10 per cent. solution of cuprous chloride in hydrochloric acid which has been previously heated almost to boiling. Each drop of the diazobenzene solution produces a yellow precipitate, which however immediately disappears with evolution of nitrogen and deposition of an oil. Subsequent distillation in a current of steam yields about 26 grams of chlorobenzene.

According to Feitler (*Z. physik. Ch.* **4**, 68), the cuprous chloride solution for Sandmeyer's reaction is best prepared thus: Crystalline sulphate of copper (250 parts), sodium chloride (120 parts), and water (500 parts) are heated to boiling, and concentrated hydrochloric acid (1,000 parts) and copper turnings (130 parts) are added. The mixture is heated in a loosely-stoppered flask till it loses its colour. The solution is now decanted, leaving undissolved copper and some sediment behind, into a tared bottle previously filled with carbon dioxide. The weight is now made up to 2,036 parts by the addition of concentrated hydrochloric acid, and a solution containing about 10 per cent. of cuprous chloride is the result. This solution can be preserved for a long time unchanged in a carefully-stoppered bottle when the air has been displaced by carbon dioxide.

Gattermann found somewhat later (*Ber.* **23**, 1,218), in attempting to prepare diphenyl by condensation from diazobenzene chloride (2 mol.) by the action of various metals, that copper in a finely-divided condition produced a specially violent action even at 0°, but instead of diphenyl, chlorobenzene was the chief product. And, continuing the investigation, he found that the amido-group in aniline and its homologues could be replaced in like manner by Br and CN, and even by the nitro-group and the radical of sulphocyanic acid.

This method reminds one at once of the Sandmeyer reaction, but possesses certain advantages over the latter. Thus, since it

uses cold solutions, the heating of large quantities of liquids is avoided. The yields are also frequently better, and while Sandmeyer's method demands the preparation of the cuprous salt of the acid whose radical is to be introduced, Gattermann's reaction dispenses with this preliminary.

The finely-divided copper used in decomposing the diazo-bodies is prepared by the action of zinc dust on cupric sulphate. A cold saturated solution of the latter is placed in a porcelain dish, and the zinc dust is shaken into it through a fine sieve while the liquid is thoroughly stirred, these precautions being taken to prevent the formation of lumps. The addition ceases when the liquid retains only a trace of blue colour. By this time the temperature will have risen to about 80° . The copper, in the state of fine powder, settles to the bottom of the vessel in a dark, red-coloured layer. It is washed as well as possible with water, and then, to remove traces of zinc, is covered with water and stirred up, while dilute hydrochloric acid is added as long as effervescence is observable. The liquid is again decanted and the precipitate washed on a filter till the washings are neutral. As it is easily oxidised, even in a nearly dry condition, it is best preserved in the form of a paste in closely-stoppered bottles.

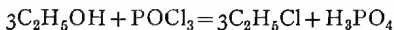
As an example of the use of Gattermann's method, the preparation of chlorobenzene may be given. Aniline ($31\text{ gr.} = \frac{1}{3}\text{ mol.}$) is dissolved in 40 per cent. hydrochloric acid (300 gr.) and water (150 cc.). Solution will not be complete; but without regard to this the mixture is cooled by throwing in pieces of ice, and diazotised by adding not too slowly a concentrated solution of sodium nitrite (23 gr.). The moist copper paste (40 gr.) is next added, and the evolution of nitrogen begins immediately. The action lasts about half an hour, and its completion is marked by the fact that the copper, at first carried to the surface by the liberated gas, finally settles to the bottom with the chlorobenzene. The greater part of the water is poured off and the chlorobenzene driven over in a current of steam. The yield is about the same as that obtained by the other copper process. The use of smaller quantities of hydrochloric acid or copper affects it unfavourably.

The yield of *o*-chlorotoluene from *o*-toluidine is 66.3 per cent. against 31.5 per cent. by Sandmeyer's method. The yields of β -chloronaphthalene from β -naphthylamine and *p*-chloronitrobenzene from *p*-nitraniline are 30 per cent. and 70 per cent. of the theoretical respectively.

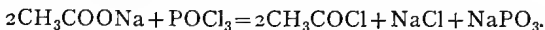
Angeli (Ber. **24** 952*c*) used solutions of sulphate of copper, to which he added the necessary amounts of the halogen acids and of sodium hypophosphite instead of employing metallic copper or Sandmeyer's solutions. He found that the preparation of chlorine, bromine, iodine, and nitro-derivatives from aniline was very satisfactory when conducted in this manner.

14. Mercuric Chloride.—When a solution of mercuric chloride in water or ether is heated with ethyl iodide in a sealed tube at 100°, ethyl chloride is formed (Schlagdenhauffen, Jahresb. **1856**, 576). According to Oppenheim (Ann. **141**, 207), this action holds generally for alkyl iodides.

15. Phosphorus Oxychloride.—This reagent, which occurs as a by-product in preparing acid chlorides with phosphorus pentachloride, and can be prepared (Odling, "Manual of Chemistry," **1**, 287) by direct union of phosphorus trichloride at its boiling-point with oxygen, may be used for the preparation of chloro-derivatives from alcohols—

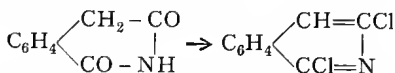


Although it has no action on free acids, Chiozza (C. R. **36**, 655) has found that it does react with their sodium salts. Geuther (Ann. **123**, 114) finds that sodium metaphosphate is formed as a result of the action—



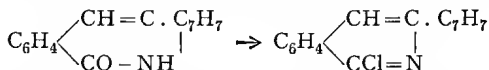
The operation is carried out by adding the oxychloride to the finely-powdered sodium salt in a flask connected with a return condenser. After the chemical action has begun, the mixture is heated for a short time in a water bath.

Quite recently Gabriel (Ber. **19**, 1,655) has used the oxychloride for removing the oxygen from homo-*o*-phthalimide, which contains the arrangement of carbon and nitrogen atoms peculiar to isoquinoline. By heating the imide (8 gr.) in a sealed tube with phosphorus oxychloride (24 gr.) for three hours at 150–170°, it was converted into dichloroisoquinoline—

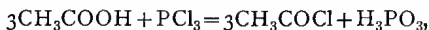


which separated out in crystalline form when the contents of the tube were poured into five times their volume of alcohol (Ber. **19**, 2,355).

Ruhemann (Ber. **24**, 3,975) heated iso-*p*-xylalpthalimidine with twice its weight of phosphorus oxychloride for half an hour in the water bath. On adding alcohol the excess of oxychloride was decomposed, and a crystalline substance began to appear, which increased in quantity on the addition of water. The resulting product was α -chloro- β -*p*-tolylisoquinoline—



16. Phosphorus Trichloride.—This reagent is used like the last for the conversion of alcohols into chloro-derivatives. It likewise converts acid into acid chlorides—



a reaction first noticed by Béchamp (C. R. **42**, 224). Its action is less violent than that of the pentachloride; but the non-volatile phosphorus acid, arising as a by-product in place of the volatile oxychloride, is sometimes hard to separate from acid chlorides which cannot be distilled without more or less decomposition. On the other hand, three molecules of acid chloride are obtained with one of the trichloride, while the pentachloride yields but one.

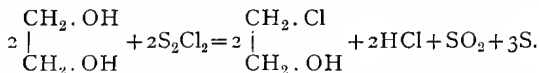
17. The Chlorides of Sulphur.—Heintz, and later Carius, (Ann. **122**, 73) recommended the use of the *monochloride*, S_2Cl_2 , for the preparation of dichlorhydrin from glycerol, and it is still used for the purpose, although it has, until lately, received no other such application. According to Claus (Ann. **168**, 43), the action which takes place is represented by the equation—



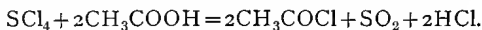
The operation is carried out as follows: About 800 grams of glycerol, boiling at 195° (?)—Rössing (Ber. **19**, 64) recommends anhydrous glycerol boiling at 176 – 177° for the purpose—are placed in a two-litre flask, which is connected with a condenser. While this is heated in a brine bath and continuously agitated, 2 kilograms of chloride of sulphur are added. After the heating has continued for 7–8 hours the action is complete, and the condenser is removed so as to allow sulphurous acid and hydrochloric acid to be driven off during a final hour's heating. On cooling, the mass becomes pasty. Two or three times its volume of ether is added, the mixture is filtered, and the filtrate distilled. After repeated rectification, pure dichlorhydrin, boiling at 179° , is obtained.

Morley (Ber. **13**, 222) states that the yield is more than 50 per cent. of the theoretical.

With glycol, chloride of sulphur gives ethylene chlorhydrin, but the product cannot be freed from impurities containing sulphur. The action may be represented thus :



Sulphur tetrachloride acts on acetic acid according to the equation—



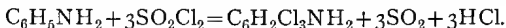
Anger and Béhal (Bull. Ch. [**3**], **2**, 144) describe the operation as follows : Glacial acetic acid and sulphur, or chloride of sulphur, in the proportion of two molecules of the former to one of the latter, are placed in a flask surrounded by a freezing mixture, and chlorine gas is led in till it is no longer absorbed. The mass, after having reached the ordinary temperature, is heated and distilled with the aid of a good condenser. The distillate is caught in a receiver surrounded by ice, as otherwise the streams of sulphur dioxide and hydrochloric acid may carry off much of the acetyl chloride. The part passing over below 60° is rectified, shaken with mercury or finely-divided copper, to remove an impurity containing sulphur, and finally redistilled. From 600 grams of the acid about 500 grams of the chloride are obtained.

When the mixture of acetic acid and sulphur is boiled during the absorption of the chlorine, the chief product is monochloroacetic acid, and but little acetyl chloride is formed. As the investigators obtained 1 kilogram of monochloroacetic acid from 800 grams of acetic acid in a single day, this is probably the best way of preparing the former substance.

18. Sulphuryl chloride.¹—This substance has been frequently

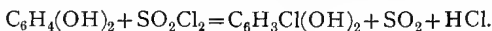
¹ It may be of interest here to describe the best way of preparing sulphuryl chloride, as it depends on a peculiar contact effect of an organic body. According to Schulze (J. pr. Ch. **132**, 168), when camphor is treated with sulphur dioxide it becomes moist on the surface and finally melts to a clear liquid (this was observed earlier by Bineau, Ann. Ch. Ph. [**3**], **24**, 326), which continues to absorb sulphur dioxide up to 0.88 of the weight of the original camphor at 725 mm. pressure. This liquid is now cooled with ice and saturated with chlorine. When the camphor, by a

used for preparing chlorinated compounds. Thus Wenghöffer (J. pr. Ch. **124**, 449) took a measured quantity of the chloride, and allowed the equivalent amount of aniline, diluted with six times its weight of ether, to drop into it. The resulting mixture became solid, and after somewhat laborious purification by recrystallisation, trichloroaniline was isolated—

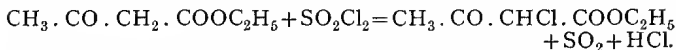


The yield was only 15 per cent. of the theoretical.

Reinhold (J. pr. Ch. **125**, 322) dissolved resorcinol in three times its weight of ether, and allowed sulphuryl chloride to flow, drop by drop, into the mixture. By fractional distillation, an amount or monochlororesorcinol equal to the resorcinol taken was obtained—



By adding sulphuryl chloride to acetoacetic ether, Allihn (Ber. **11**, 569) obtained a liquid consisting almost entirely of monochloroacetoacetic ether boiling between 193° and 195° —



Similarly Roubloff (Ann. **259**, 254) added sulphuryl chloride (1 mol.) slowly to well-cooled methylacetoacetic ether. The action began when one third of the quantity had been added, and the evolution of hydrochloric acid and sulphur dioxide continued till the mixing was completed. The mixture was warmed on the water bath for a short time, diluted with ether, and washed with water until neutral. The ethereal solution was dried with calcium chloride, and, after fractionation, yielded pure chloromethylacetoacetic ether.

19. Chlorsulphonic Acid, HClSO_3 .—This and the succeeding substances are used to a very limited extent only.

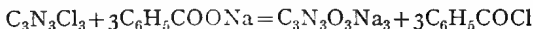
Chlorsulphonic acid is not suited for the preparation of simple acid chlorides, but it has been used by Heumann and Köchlin,

continuation of this alternating treatment, has taken up twice its weight of sulphuryl chloride, both gases can be led in together. If the column of liquid be tall enough, and care be taken that the tubes leading the gases distribute them through the liquid, very rapid streams of gas will be perfectly absorbed. The sulphuryl chloride is distilled off at as low a temperature as possible (it boils at 77°), to avoid the carrying over of more than a trace of camphor. The presence of this is shown by the white flakes which remain suspended when the substance is shaken with water.

(Ber. **15**, 1,166) for the conversion of aromatic sulphonic acids into sulphonic chlorides. Thus they mixed *p*-toluenesulphonate of sodium (97 gr. = 1 mol.) with chlorsulphonic acid (58.25 gr. = 1 mol.), and poured the mixture into water. Toluenesulphonic chloride (36.5 gr.) was deposited.

20. Thionyl Chloride, SOCl₂.—Thionyl chloride was tested by the same authors (Ber. **16**, 1,627), with regard to its action on several organic acids. Butyric acid (10 gr.) reacted at once, giving butyryl chloride (6 gr.). Benzoic acid (10 gr.) boiled with thionyl chloride, with use of a return condenser, gave benzoyl chloride (10 gr.). The yields obtainable seem to be good.

Cyanuric chloride acts on sodium salts of acids when heated with them for several hours in sealed tubes at 100°, producing acid chlorides. The yield from sodium acetate, according to Senier (Ber. **19**, 310) is only 22 per cent. of the theoretical, while sodium benzoate gives 88 per cent. The equation—



represents the course of the interaction.

SECTION III.—IODO-DERIVATIVES.

Although iodine is frequently used alone in the solid form for the preparation of iodo-derivatives, it is most frequently employed in the presence of oxidising agents or of phosphorus.

As solvents alcohol, ether, chloroform, carbon disulphide, potassium iodide solution, hydriodic acid, benzene, toluene, and other substances are used.

Among the less commonly used agents for the production of iodo-derivatives are iodine chloride, phosphonium iodide, and iodide of nitrogen.

The chlorine or bromine in substances containing these elements can often be replaced by iodine by the action of potassium, sodium, or silver iodides.

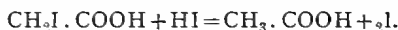
Iodo-derivatives are likewise obtained by the action of hydriodic acid on several classes of bodies, and by addition of that substance and of iodine and iodine chloride to unsaturated bodies.

1. Free Iodine.—Fischer (Ann. **211**, 233) found that toluene was not attacked by iodine in solution in chloroform or carbon disul-

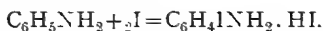
phide, but that when they were heated alone to the melting-point of iodine, a violent action took place and the mixture became crystalline on cooling. Cold chloroform removed unchanged toluene and iodine, and the residue after recrystallisation proved to be toluene di-iodide, $C_{14}H_{10}I_2$. The addition of ferrous iodide or mercuric oxide would doubtless be advantageous in cases like this (cf. § 4).

Birnbaum and Reinherz (Ber. **15**, 457) obtained iodobenzoic acid and di-iodosalicylic acid by the action of iodine on the dry silver salts of benzoic and salicylic acids. The yield was poor however. Birnbaum had previously observed (Ann. **152**, 116) that no iodoacetic acid could be obtained from silver acetate by this method.

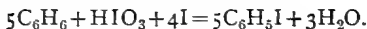
In spite of its general resemblance to chlorine and bromine, iodine never produces substitution products by acting on dissolved organic bodies. Kekulé was the first (Ann. **131**, 122) to discuss this peculiarity fully. The cause is to be found in the fact that the hydriodic acid arising from the action immediately decomposes the derivative, or even prevents its formation. Kekulé proved that when iodoacetic acid is mixed with concentrated hydriodic acid in the cold, iodine is deposited and acetic acid is formed—



On the other hand this very fact explains why bases can be converted into iodo-derivatives with ease, for they unite at once with the hydriodic acid as soon as it is set free. Thus aniline gives directly iodoaniline hydriodide—

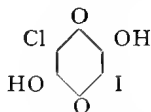


Kekulé suggested later (Ann. **137**, 162) the use of *iodic acid* to destroy the influence of the hydriodic acid by oxidising its hydrogen, when non-basic bodies were in question. Thus by heating benzene (20 gr.), iodine (15 gr.), and iodic acid (10 gr.) at 200–240° in a sealed tube, he obtained iodobenzene—



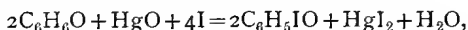
A modification of this method is to dissolve iodine and iodic acid in a very dilute caustic potash, and add the solution to the acid reacting substance—e.g. phenol, into which the iodine is to be introduced, and then mix with the necessary amount of hydrochloric acid. Derivatives containing more iodine can be obtained by using the proper molecular amounts of iodine and iodic acid.

Kehrmann and Tiesler (J. pr. Ch. **148**, 437) prepared iodo-chlorodioxyquinone,

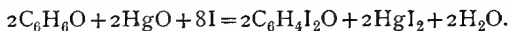


by dropping potassium iodide and iodate, mixed in the proper proportions, into a strongly acid solution of chlorodioxyquinone. The free iodine formed at first disappears almost immediately, and after a short interval a crystalline powder, consisting of an almost quantitative yield of the desired substance, is precipitated.

Hlasiwetz and Weselsky (Centralblatt, **1870**, 63) recommend the use of an easily reducible oxide of a metal whose iodide is insoluble, in place of iodic acid. They state that *mercuric oxide*, prepared in the wet way, is best suited to this purpose. Thus iodine and mercuric oxide are thrown in small quantities at a time, with continual agitation, into an alcoholic solution of phenol, so much mercuric oxide being always taken that the brown colour of the solution disappears. The reaction proceeds rapidly, and the natural warming of the solution is moderated by external cooling. When the ingredients are used in the proportions required by the equation—



some di-iodide is formed at the same time. The di-iodide is almost the sole product when the proportions used correspond to the equation—

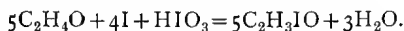


Töhl (Ber. **25**, 1,522) mixed iodine (25 gr.), petroleum ether (250 cc.), durene (20 gr.), and mercuric oxide (11 gr.), and, after allowing them to remain together for three weeks, washed the solution with sodium hydroxide. On distilling off the petroleum ether and fractionating the residue, he obtained iododurene (cf. § 4).

Stenhouse dissolved orcinol in ether (6 parts), added iodine (2 parts), shook the mixture till all the iodine had dissolved, and then added finely powdered litharge. A violent action took place, and iodo orcinol, $\text{C}_7\text{H}_7\text{IO}_2$ was formed.

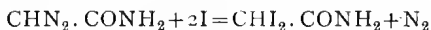
Clermont and Chautard (C. R. **100**, 745) state that when acetone (200 gr.), iodine (100 gr.), and iodic acid (40 gr.), are allowed to stand for eight days, and the mixture is then heated, with reflux condenser,

for two to three hours, addition of water precipitates iodoacetone, C_3H_5IO . This is a very unstable substance. They found also (C. R. **102**, 119) that, using the same method with aldehyde, if the mixture remained until the iodine had completely disappeared, iodoaldehyde was formed according to the equation—



2. Iodine with Solvents.—In connection with the discussion of the use of solvents for iodine, it may be pointed out that, as many liquids dissolve iodine, the substance to be acted upon will frequently have this property, and so the addition of a special solvent will be unnecessary.

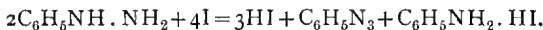
Curtius (Ber. **18**, 1,285) dissolved iodine and diazoacetamide in *alcohol* and obtained di-iodoacetamide.



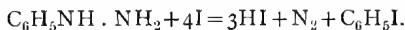
Schall (Ber. **16**, 1,897) suspended perfectly dry phenol-sodium (20 gr.) in *carbon disulphide* (300 cc.) and added iodine (45 gr.) gradually. A large quantity of iodophenol was formed at once, although its separation from other products presented considerable difficulties.

Baeyer (Ber. **18**, 2,274) added a solution of iodine in *potassium iodide* to the undried copper compound of propargylic ether as long as the colour of the iodine continued to disappear rapidly after each addition. The resulting precipitate, after being pressed free from water and moistened with a few drops of alcohol, was extracted twenty times with ether. The extract deposited on evaporating iodopropargylic ether, $I-C \equiv C-COOC_2H_5$.

According to Fischer (Ber. **10**, 1,335), the interaction of phenylhydrazine and iodine produces chiefly hydriodic acid, diazobenzene imide, and aniline—



Meyer (J. pr. Ch. **144**, 115) finds, however, that this only holds in the presence of excess of phenylhydrazine. If iodine (2 mol.) and phenylhydrazine (1 mol.) are taken, iodobenzene is produced and nitrogen gas escapes.

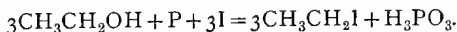


Meyer dissolved iodine (18.5 gr.) in potassium iodide solution, and added slowly to this a solution of phenylhydrazine (4 gr.) in much water. The action was completed by warming for a short time in the water bath. A

dark-coloured oil was deposited, which, on being dried and distilled, was found to consist mainly of iodobenzene. The yield was 6.5 grams in place of 7.4 grams. The reaction became quantitative when a very dilute solution of iodine ($\frac{1}{10}$ normal) was used.

When *excess of iodine* has been added, the unused part can be removed by steam, potassium iodide solution, or mercury, when it is unadvisable to employ an alkali for the purpose. Partheil (Ber. **24**, 636) decolourised a solution containing iodine with carbon disulphide, and expelled the excess of the latter with carbon dioxide.

3. Iodine Carriers—Phosphorus.—This substance is principally used in preparing iodides of hydrocarbon radicals from alcohols.



The method was discovered by Serullas (Ann. Ch. Ph. **25**, 223).

Hofmann (Ann. **115**, 273) describes the use of *yellow phosphorus* in this connection as follows: The phosphorus is placed in a retort whose neck is connected with a condenser. One quarter of the alcohol to be used is poured on to the phosphorus through a funnel, provided with a stop-cock, and passing through a cork in the tubulus of the retort. The apparatus is placed on a water bath, and, the iodine having been dissolved in the remainder of the alcohol, the solution is allowed to flow in slowly through the funnel. The interaction begins immediately, and almost as fast as the liquid enters through the funnel a mixture of alcohol and ethyl iodide distills over into the receiver. As iodine is not very soluble in alcohol, a good deal which the alcohol at disposition has not been able to dissolve will always remain over. It is very soluble in ethyl iodide, however, so the first part of the distillate is used to dissolve the residue, and this is allowed to flow into the apparatus once more, when the remaining iodine is almost immediately converted into ethyl iodide. The distillate is washed with water, dried and rectified. With proper proportions such as iodine (1,000 gr.), methyl alcohol (500 gr.), and phosphorus (60 gr.), a yield equal to 94–95 per cent. of the theoretical may be attained.

Ethyl iodide, which was first made by Gay-Lussac in 1835, requires iodine (1,000 gr.), alcohol (700 gr.), and phosphorus (50 gr.) The yield is 96–98 per cent., on account of the smaller volatility of the ethyl iodide.

Beilstein (Ann. **126**, 250) gives the method of using *red phosphorus* as follows: In a retort connected with a return condenser

are placed red phosphorus (10 parts) and alcohol, sp. gr. 0·83 (50 parts). Iodine (100 parts) is then thrown in in small portions at a time, and after the mixture has remained for twenty-four hours the ethyl iodide is distilled off. The distillate is treated with a trace of caustic soda to precipitate any dissolved ethyl iodide, and at the same time to decolourise the product. A second distillation gives the pure substance in almost theoretical quantity. The red colour, which ethyl iodide always acquires on standing, may be hindered from appearing by placing a clean piece of copper wire in the bottle.

Walker (J. Ch. Soc. **61**, 717) recommends a method which does away with the tediousness of the gradual addition of iodine. The iodine is placed, 100 grams at a time, in an apparatus similar to those used in fat extraction, placed between the flask, containing the phosphorus and alcohol, and the condenser. The flask is charged with equal parts of red and yellow phosphorus. The yield is 570 grams of ethyl iodide from 500 grams of iodine.

V. Meyer (Ber. **19**, 3,295) gives the following method of making β -iodopropionic acid. Glycerol is oxidised in the usual manner with nitric acid (cf. Chap. XVIII.), and the liquid is evaporated and the nitric acid expelled on the water bath. The sirup which results is diluted to a sp. gr. 1·26, and is poured 30 cc. at a time on iodide of phosphorus, which has meanwhile been prepared by mixing iodine (50 gr.) and yellow phosphorus (6·5 gr.) in a flask. If the action does not begin of itself, it is started by gentle heating. After the violence of the action has abated the mixture is allowed to cool, and in doing so forms a mass of almost colourless plates of iodopropionic acid. The substance may be made perfectly pure by recrystallisation from water, but is sufficiently pure for most purposes after simple pressing and drying.

In the case of *solid alcohols*, the substance is melted with the red phosphorus and the iodine added to the fused mass. Thus Hell and Hägele (Ber. **22**, 503) heated myricyl alcohol with ordinary phosphorus in an oil bath to 130–140°, and added iodine in small portions until violet vapours began to be continuously emitted. The heating was carried on as long as gases were evolved, and finally the cold reddish-brown mass was extracted with boiling water. The residue, consisting of myricyl iodide, was recrystallised from alcohol and petroleum ether.

4. Iodine Carriers—Ferrous Iodide.—Besides phosphorus, ferrous iodide is used as an iodine carrier, while *aluminium iodide* and *ferric chloride* are less useful in this respect.

Here also the method of *melting solid alcohols* with iodine and the iodine carrier is useful. Thus when phenylpropionic acid (20 gr.) was allowed to remain in contact with iodine in carbon disulphide solution, only 1.5 grams of the di-iodide were formed. But by mixing the acid with the molecular proportion of iodine, adding a little ferrous iodide, and keeping the whole for an hour at 140–145°, Liebermann and Sachse (Ber. **24**, 4,113) obtained di-iodo-phenylpropionic acid very readily. The corresponding compound of behenic acid is formed even at 100°.

Iododurene, whose somewhat complicated preparation in the wet way has already been explained, can be made with the utmost ease by melting durene and iodine and gradually adding mercuric oxide until the halogen has disappeared (Ber. **25**, 1,523).

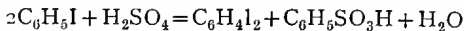
Anhydrous ferrous iodide has likewise been used in producing iodides in the wet way. Thus Liebermann and Sachse (Ber. **24**, 4,113) dissolved phenylpropionic acid and iodine in cold carbon disulphide, and added one-tenth as much ferrous iodide as of the acid. After twenty-four hours 3.5 grams of the iodide had been formed, and in ten days the action was practically complete.

Lothar Meyer (Ann. **231**, 195) showed that, in presence of *ferric chloride*, the action of iodine on benzene probably takes place according to the equation—



The course of the action is therefore rather complicated, and appears also to be somewhat uncertain. Gustavson (Ber. **9**, 1,607) has shown that *aluminium iodide* is of little use for the present purpose.

5. Application of Sulphuric Acid.—According to Neumann (Ann. **241**, 37), sulphuric acid is, in a sense, an iodine carrier, since by its aid many monoiodo-compounds can be converted into di-iodo-compounds. Thus when iodobenzene (50 gr.) was added to concentrated sulphuric acid (50 gr.), and the mixture warmed and frequently agitated for two hours at 170°, cooling caused a separation of crystals which, after washing with water and purification, were found to be *p*-di-iodobenzene (20 gr.). The equation



explains its formation. Iodotoluene and iodophenol gave corresponding di-iodo-derivatives.

Hammerich (Ber. **23**, 1,635) covered iodo-*m*-xylene with three

times its weight of concentrated sulphuric acid, and allowed them to remain in contact, with frequent shaking, for six weeks. The upper layer, consisting of sulphuric acid, was then poured off, and the lower layer was washed with water, decolourised with sodium thiosulphate, and distilled *in vacuo*, when di-iodoxylene was obtained.

6. Use of a Solution of Iodine in Potassium Hydroxide.—

Messinger and Vortmann's method (Ber. **22**, 2,312) is based on this, and gives excellent yields of iodophenols. An alkaline solution of the phenol is heated to 50–60°, and an excess of iodine (8 atoms iodine to 1 mol. phenol dissolved in 4 mol. potassium hydroxide) is added. A dark-red precipitate is produced, which is almost entirely soluble in caustic potash. Precipitation with acids gives tri-iodophenol, $C_6H_3I_3O$. Thymol gives, with the same treatment, the di-iodo-derivative $C_{10}H_{12}I_2O$.

It is noteworthy that a slight modification of this process leads not only to the replacement of the hydrogen atoms in the nucleus, but also of that in the hydroxyl group. Thus iodothymol iodide (Ger. Pat. 49,739) is obtained by allowing a solution of iodine in potassium iodide or a solution of iodine in caustic potash, to which an agent for setting the iodine at liberty, such as chlorine or bleaching-powder, had been added, to flow into an alkaline solution of phenol at 10–30°. The iodide of iodosalicylic acid (Ger. Pat. 52,833) and similar compounds can be made in the same way.

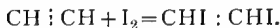
7. Addition of Iodine.—

All *alkaloids take up iodine* and iodine chloride (cf. § 10) directly, when solutions of the salts of the alkaloids are mixed with the proper amount of iodine dissolved in potassium iodide. Thus Jörgensen (J. pr. Ch. **109**, 433) obtained tarkonine heptiodide, $C_{12}H_{12}NO_3I_7$. The tetra-alkylammonium derivatives possess the same property as is shown by the existence of Marquart's tetra-ethylammonium tri-iodide (J. pr. Ch. **110**, 433). Einhorn (Ber. **20**, 1,221) precipitated anhydroecgonine almost quantitatively as periodide¹ by means of a solution of iodine in hydriodic acid.

¹ It is worthy of mention that alkaloids likewise form addition products with hydrogen polysulphide. For example, Schmidt (Ar. Pharm. **25**, 149) found that when yellow ammonium sulphide was added to a warm alcoholic solution of berberine hydrochloride or sulphate, brown crystals

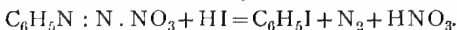
Metallo-derivatives of acid amides seem to possess the same property, according to Tafel and Enoch (Ber. **23**, 1,552). They prepared acetamidomercuric iodide, $(\text{CH}_3\text{CONH})_2\text{HgI}_2$, and other similar compounds.

Finally, iodo-derivatives are obtained by the addition of iodine to *unsaturated bodies*. Only two atoms, however, can be added to a triple linkage. Thus, when acetylene is led into a solution of iodine in absolute alcohol, ethylene di-iodide is formed—



Even if propargylic acid (Ber. **24**, 4,120), $\text{CH} : \text{C} \cdot \text{COOH}$, is heated in chloroform with two molecules of iodine for six hours at 100° , nothing more than di-iodoacrylic acid is obtained.

8. Action of Hydriodic Acid.—Griess first showed that hydriodic acid acts on *diazo-bodies* producing iodo-derivatives.



Thus Gabriel and Herzberg (Ber. **16**, 2,037) diluted hydriodic acid with an equal volume of water, and warmed the nitrate of *o*-diazocinnamic acid with four times its weight of the diluted acid until the evolution of nitrogen ceased. On adding more water, filtering and washing with a little sodium thiosulphate to remove free iodine, and finally recrystallising, pure iodocinnamic acid, $\text{IC}_6\text{H}_4 \cdot \text{C}_2\text{H}_2 \cdot \text{COOH}$, was obtained.

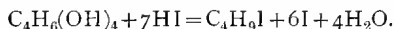
This reaction sometimes goes with unexpected smoothness, as in a case where Hähle (J. pr. Ch. **151**, 72), following the directions of Schmitt (Ber. **1**, 68), treated nitrodiazophenol chloride with hydriodic acid. The action was too violent at ordinary temperatures, so he added the diazo-compound gradually to a suitable amount of ice-cold hydriodic acid. After the last traces of nitrogen had been driven off by warming, idonitrophenol was precipitated quantitatively by adding water.

Sandmeyer's and Gattermann's methods (cf. Chap. XVI, Sections I and II) can of course be used for preparing iodo-derivatives. The latter prepares iodo-benzene by taking aniline (31 gr.), concentrated sulphuric acid (200 gr.), water (200 cc.), sodium nitrite (23 gr.), potassium iodide (126 gr.), and finely divided copper (40 gr.). The yield, 48 grams of iodobenzene, corresponds to 70 per cent. of the theoretical.

of a berherine polysulphide, $(\text{C}_{20}\text{H}_{17}\text{NO}_4)_2\text{H}_2\text{S}_6$, came out. Strychnine gives under the same conditions, $(\text{C}_{21}\text{H}_{22}\text{N}_2\text{O}_2)_2\text{H}_2\text{S}_6$.

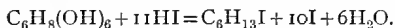
Higher alcohols as well as *secondary* and *tertiary alcohols* give iodo-derivatives directly on being treated with hydriodic acid. Thus Freund and Schönfeld (Ber. **24**, 3,354) warmed octylic alcohol on the water bath, the action being too weak in the cold, and conducted into it hydriodic acid. This was rapidly absorbed, and the current of gas was continued until a yellow layer of the acid began to accumulate on the bottom of the vessel, and the liquid smelt very strongly of the same substance. As the iodide decomposes on distilling, it was simply decolourised by shaking with sodium bisulphite. A yield of 180 grams of $\text{CH}_3\cdot\text{CHI}\cdot\text{C}_6\text{H}_{13}$ was obtained from 100 grams of the alcohol.

Tertiary butyl alcohol $(\text{CH}_3)_3\text{COH}$ gives tertiary butyl iodide, according to Butlerow (Ann **144**, 5), when saturated with hydriodic acid gas, or shaken with a concentrated solution of the acid. The product is decolourised by shaking with caustic potash or potassium bisulphite and distilled. Erlenmeyer (Ann. **126**, 305) states that when glycerol is boiled with excess of hydriodic acid, isopropyl iodide is formed. It should be noticed that when polyhydric alcohols are treated in this manner, secondary iodides are always formed. Thus erythrol gives secondary butyl iodide.



Iodo-alcohols cannot be prepared in this way, as the hydriodic acid attacks all the hydroxyl groups at once. Iodo-derivatives of the hydrocarbons are always obtained instead.

In connection with this method one more example, Munsche's (Dissert. Jena, 1890) preparation of hexyl iodide, may be described. He makes part of the hydriodic acid during the process out of iodine, phosphorus, and water, an operation which is facilitated by the presence of iodine produced by the action itself.



Iodine (200 gr.) and hydriodic acid sp. gr. 1.7 (100 gr.) are placed in a tubulated retort, and red phosphorus (90 gr.) is added. At first the part of the phosphorus necessary just to decolourise the solution is taken, and then, while the vessel is gently warmed on a sand bath, the rest of the phosphorus is added in small portions alternately with portions of mannitol (120 gr.). After two thirds of the latter has been used, the rest of the phosphorus and mannitol, together with the portion of hexyl iodide mixed with hydriodic acid which has meanwhile distilled over, are introduced into the retort. The resulting iodide is first distilled in a current of steam, and then by itself. The yield is said to be good.

Leser (Ber. **17**, 1,826) prepared *o*-xylilene iodide, $C_8H_8I_2$, by boiling phthalyl alcohol with fuming hydriodic acid and a little red phosphorus. The iodide was extracted from the solution, after dilution with water, by means of ether.

Iodine was introduced in place of chlorine by means of hydriodic acid by Friedländer and Weinberg (Ber. **18**, 1,531). On heating *a*-chloroquinoline at 240° with acetic acid and hydriodic acid, quinoline itself was formed, but by altering the conditions of the action the intermediate *a*-iodoquinoline was obtained. For this purpose chloroquinoline was heated with hydriodic acid (b.-p. 127°) and a little amorphous phosphorus at 140 - 150° for three hours. On cooling, the contents of the tube deposited crystals of *a*-iodoquinoline hydriodide.

Finally, it should be mentioned that diazo-bodies containing chlorine, bromine, or iodine give *mixed halogen derivatives*. Thus Silberstein (J. pr. Ch. **135**, 119) found that on adding concentrated hydriodic acid to an aqueous solution of tribromodiazobenzene nitrate, nitrogen was rapidly evolved, and tribromiodobenzene deposited.

9. Addition of Hydriodic Acid to Unsaturated Bodies.—

Hydriodic acid unites with unsaturated substances much more easily than hydrochloric or hydrobromic acids, and forms iodo-derivatives.

Thus Markownikoff (Z. Ch. **1870**, 423) prepared iodopropyl

alcohol, C_3H_7IO , as follows: Propylene oxide, $CH_3-\overset{\text{O}}{\text{CH}}-\text{CH}_2$, was diluted with a little more than an equal amount of water, and hydriodic acid was conducted through a tube just to the surface of the liquid. As soon as the solution acquired a strongly acid reaction it was diluted with more water. The iodopropyl alcohol, which was thrown down, was then purified by fractionation *in vacuo*.

A common method is to dissolve the unsaturated substance in acetic acid and add a solution of hydriodic acid in the same solvent, then, after heating if necessary, to pour the mixture into water, when the product separates out.

Lippmann (C. R. **53**, 968) obtained iodo-alcohols directly from unsaturated hydrocarbons by addition of hypoiodous acid, or its elements, at the moment of its formation. Thus by dissolving

iodine and amylene in chloroform in presence of freshly precipitated mercuric oxide, he obtained from the solution a heavy yellow oil which turned out to be a mixture of different iodoalcohols.

Melikoff obtained iodolactate of potassium by the action of fuming hydriodic acid on the dry potassium salt of glycidic acid.

10. Addition of Iodine Chloride.—The chloride (and bromide) of iodine give mixed halogen derivatives by addition. Dittmar (Ber. **18**, 1,612) mentions particularly its power of combining with alkaloids. He states that the number of molecules of the halogen compound taken up corresponds with the number of pyridine rings in the compound. He prepared his iodine chloride solution by mixing potassium iodide, sodium nitrite, and hydrochloric acid, or by conducting chlorine into water containing suspended iodine.

Iodine chloride was first used for producing iodo-derivatives by Brown (Phil. Mag. [4] **8**, 201), and later by Stenhouse (J. Ch. Soc. **17**, 327; Ann. **134**, 219). The latter found however that, while iodine was often introduced, the chlorine frequently acted as if it had been alone present and free iodine separated out.

Michael and Norton (Ber. **9**, 1,752) have revived its claims to be considered a good reagent for producing iodo-compounds. They prepared it by passing a stream of dry chlorine over iodine, until the weight of the latter had increased by a little less than the calculated amount. Acetanilide (Ber. **11**, 108) was dissolved by them in much glacial acetic acid, and iodine chloride was added. A good deal of iodoacetanilide separated out at once, and the rest was precipitated on addition of water. The yield was 89-90 per cent of *p*-iodoacetanilide. They likewise prepared di-iodoaniline by dissolving aniline in several times its volume of acetic acid, and leading into it gaseous iodine chloride (2 mol.). With a solution of aniline in hydrochloric acid and the necessary amount of iodine chloride (3 mol.) they obtained tri-iodoaniline (yield 15 per cent.).

Völker (Ann. **192**, 90) dissolved solid iodine trichloride (96 gr.) in a litre of water, added acetone (48 gr.), warmed the whole to 66°, when cloudiness appeared, and finally cooled again to the ordinary temperature. An oil was deposited from which di-iodoacetone was separated. From 5,225 grams of iodine trichloride

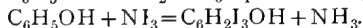
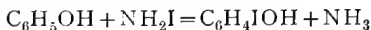
and 2,600 grams of acetone he obtained, after elaborate purification, 1,020 grams of the crude product. An examination of the by-products led him to give the following equation for the action :—



Green (C. R. **90**, 40) caused iodine chloride to act on benzene containing some aluminium chloride, and obtained iodobenzene along with products containing more iodine.

11. Phosphonium Iodide and Iodide of Nitrogen.—Girard (C. R. **101**, 478) states that phosphonium iodide and ethylene oxide give ethylene iodide and phosphine.

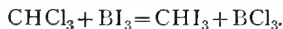
Willgerodt (J. pr. Ch. **147**, 290) found that phenols could be easily converted into iodo-derivatives by means of the iodides of nitrogen, and he devised a method by which the separate preparation of these bodies could be avoided :—



Thus for preparing iodo-thymol he dissolved thymol (5 gr.) in ammonia (6 cc.) and alcohol (2 cc.), and added gradually powdered iodine (8.5 gr.). On addition of water the product was precipitated (yield 45 per cent.). A di-iodo-derivative could not be obtained by this method. But with *o*-cresol di-iodocresol was the chief product. Rise in temperature must be prevented, as otherwise tarry matters are formed. Experiments with polyatomic phenols were unsuccessful.

12. Action of Boron Tri-iodide and Iodides of Calcium, Sodium, and Potassium on Chloro-Derivatives.—Perkin and Duppa (Ann. **112**, 125) were the first to show that such compounds as these could be used for the purpose of replacing chlorine by iodine.

Boron tri-iodide has the property of converting chloroform into iodoform when the substances remain in contact for several days (Moissan, C. R. **113**, 19).



It likewise changes carbon tetrachloride into carbon tetriodide, a substance which can hardly be obtained in any other way.

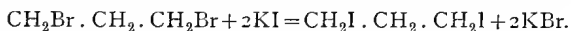
Lothar Meyer (Ann. **225**, 166–170) investigated thoroughly the

exchange of chlorine, bromine, and iodine between organic and inorganic bodies, and gave a list of all previously recorded cases. Later Spindler (Ann. **231**, 258) found that while dried *calcium iodide* had no action, the common form of the salt, containing a little less than four molecules of water of crystallisation, could transform all liquid chloro- and bromo-derivatives into corresponding iodo-derivatives. Unfortunately the slowness of the action and the frequent poorness of the yield diminish the value of the method.

In using this process, the substance (carefully dried) is placed in a dry sealed tube with calcium iodide and exposed to a temperature of 70-75° for 120 hours. For example, chloroform (1.35 gr.) and calcium iodide (5 gr.) gave 17.4 per cent. of iodoform; carbon tetrachloride (2.3 gr.) gave 14.4 per cent. of carbon tetriodide. But if sufficient time is allowed the action in the latter case becomes almost quantitative. Ethylene chloride gave 86 per cent. of ethylene iodide.

Sodium iodide is preferred to the potassium salt for actions like the present because it is easily soluble in strong alcohol. Liebig and Wöhler (Ann. **3**, 266) obtained benzoyl iodide by distilling benzoyl chloride with potassium iodide, a process which is still the only one for making acid iodides.

According to Perkin (Ber. **18**, 221), when trimethylene bromide, dissolved in alcohol, is treated with excess of potassium iodide, (sodium iodide would probably work better), it is transformed almost quantitatively into the iodide.



It is therefore very probable that many iodo-derivatives, which can only be made with difficulty or not at all directly, can be obtained thus indirectly with ease. For example, Henry (Ber. **17**, 1,132) found that the best way to make propargyl iodide, $\text{CH} : \text{C} \cdot \text{CH}_2\text{I}$, was by the action of sodium iodide on $\text{C}_3\text{H}_3\text{Br}$ in alcoholic solution. The same observer found (Ber. **24**, 74 c) that actions of this kind are most effective in methyl alcohol as solvent. He states that under these circumstances methyl chloride can be converted almost quantitatively into the iodide by warming the mixture gently in a pressure bottle.

Claus (Ann. **168**, 24) obtained *s*-di-iodhydrin by heating, in a brine bath, dichlorhydrin with slight excess of potassium iodide and enough water to dissolve them.

Demuth and Meyer (Ann. **256**, 28) made the till then vainly

sought iodoethyl alcohol by forming a thin paste of ethylene chlorhydrin, C_2H_4ClOH (25 gr.), and finely powdered potassium iodide and heating them, with frequent agitation, on the water bath for twenty-four hours. The product was then filtered and the residue washed with ether. The filtrate was decolourised with sodium thiosulphate, and the ethereal layer having been separated was dried with dehydrated sodium sulphate. On distilling off the ether a faintly reddish oil, the iodhydrin, C_2H_4IOH (25 gr.), remained.

13. Dissimilarity in Properties of Ethyl Chloride, Bromide, and Iodide.—In connection with the subject of this chapter it may be well to mention that ethyl chloride, bromide, and iodide, which are closely allied and frequently used substances, do not by any means always act similarly towards other bodies. This is true in spite of the fact that the two last are often regarded as interchangeable.

An illustration of this difference is seen in the fact that an alcoholic solution of ethyl chloride has no action on silver nitrate even when boiled with it, while ethyl bromide under the same circumstances gives rise to ethyl nitrate and silver bromide.

Again, Fischer (Ber. 9, 885) found that when molecular proportions of phenylhydrazine and ethyl iodide were mixed heat began to be developed in a short time, and, if large quantities were used, the action became so violent that the whole of the material was decomposed with explosive evolution of gas. By substituting ethyl bromide, however, the action could be conducted by heating in connection with a return condenser on the water bath, and at the end of a few hours the interaction was complete and the solution solidified to a mass of crystals.

The difference is likewise shown in cases like the introduction of the propyl radical into benzyl cyanide. V. Meyer (Ann. 250, 153) found that propyl iodide acted very easily, while propyl bromide had no effect at all.

Henry (C. R. 96, 1,149) investigated fully the relative activity of the haloids in mixed halogen compounds, and in this connection James' (J. pr. Ch. 128, 351) synthesis of taurine from ethylene chlorobromide may also be recalled.

It may not be out of place here to remind the reader that potassium and sodium do not always behave alike towards organic bodies.

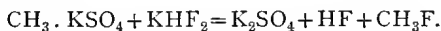
How very different their action towards the same substance may be is shown by an observation made by Merz and Weith (Ber. **6**, 1,518). They found that sodium could be kept unchanged for years in dry bromine, and could even be heated with it to 200° without much action taking place. Potassium, on the other hand, even when placed in bromine which had been perfectly dried with sodium, produced immediate ignition and explosion.

SECTION IV.—FLUORO-DERIVATIVES.

Reinsch (J. pr. Ch. **19**, 314) was the first systematically to attempt to make organic compounds containing fluorine. As early as 1840 he tried to obtain ethyl fluoride by leading hydrofluoric acid gas into absolute alcohol, but without success. Städeler (Ann. **87**, 137) showed that the solution of hydrofluoric acid in water was completely indifferent towards many organic bodies, and suggested the use of gutta-percha bottles for holding it.

Reinsch draws attention to the corrosive action on the skin of organic liquids containing hydrofluoric acid, having found that such liquids, especially if they get under the nails, produce protracted and almost unendurable pain, which can only be mitigated by dipping the members affected in ice water. Another writer recommends bathing with caustic soda.

The gaseous methyl and ethyl fluorides were made by Fremy (C. R. **38**, 393) by distilling the potassium alkyl sulphate with acid potassium fluoride.



The action is probably more complicated, however, than this equation indicates, since Seubert (Ber. **18**, 2,646), when making ethyl fluoride by this method, found that caustic alkali removed about 25 per cent. of carbon dioxide from the resulting gas.

Borodine (Repert. de Chim. **1862**, 336) obtained benzoyl fluoride as a liquid boiling at 161° by distilling benzoyl chloride with acid potassium fluoride from a platinum retort. It had but little corrosive effect on glass.

1. Interaction of Silver Fluoride with Iodo- and Chloro-Derivatives.—It is strange that silver fluoride was not used until recently for the preparation of fluoro-derivatives, seeing that, as might be expected, it yields them very readily.

Thus Moissan (C. R. **107**, 266 and 1,155) obtained ethyl fluoride by allowing a stream of ethyl iodide to flow slowly into silver fluoride. He freed the gas from the ethyl iodide, which was carried off mechanically, by passing it first through a tube cooled to 20° and then over a fresh quantity of silver fluoride.

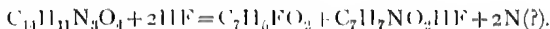
Meslans (C. R. **110**, 717) placed chloroform (1 part), iodoform (2 parts), and silver fluoride (1 part) in a flask cooled with ice. As it was allowed to become warmer, a gas was evolved consisting chiefly of fluoroform. This was purified by passage first through a tube cooled to -23° , then once more over warmed silver fluoride, and then over caoutchouc to remove chloroform vapour. After passing finally through cuprous chloride, to remove carbonic oxide, the gas was pure.

Chabrié (C. R. **110**, 1,202) prepared gaseous methylene fluoride CH_2F_2 in a similar way from methylene chloride.

2. Action of Hydrofluoric Acid on Diazo-Bodies. This method has frequently been used for the production of fluoro-derivatives. Thus, on boiling diazobenzenesulphonic acid with the ordinary solution of hydrofluoric acid in water, Lenz (Ber. **12**, 581) obtained fluobenzenesulphonic acid, $\text{C}_6\text{H}_5\text{FSO}_3\text{H}$.

Ekbom and Mauzelius (Ber. **22**, 1,846) dissolved naphthylamine in warm, strong hydrofluoric acid, and added excess of potassium nitrite dissolved in a small amount of water. Nitrogen was evolved, and a considerable amount of fluonaphthalene formed.

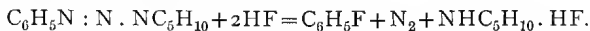
Schmitt and Gehren (J. pr. Ch. **109**, 395) added diazoamidobenzoic acid in portions of 10–15 grams at a time to 200 cc. of fuming hydrofluoric acid contained in a large platinum basin. Fluobenzoic acid was formed, along with amidobenzoic acid hydrofluoride, according to the equation



In a similar manner Mauzelius (Ber. **22**, 1,844) obtained fluonaphthalenesulphonic acid by adding α -diazonaphthalenesulphonic acid to 50 per cent. hydrofluoric acid.

As the result of some investigations on this subject, Paterno and Oliveri stated that fluorine derivatives of hydrocarbons could not be obtained by the decomposition of salts of diazo-bodies with hydrofluoric acid. But Wallach (Ann. **235**, 258) has found a means of preparing them easily and in large quantities from diazoamido-compounds. Thus by mixing solutions in water of

diazobenzene chloride and piperidine a quantitative yield of benzene diazopiperidide results. By mixing a quantity of this substance (10 gr.), after drying it in the air, with concentrated hydrofluoric acid (20–30 cc.), a violent reaction sets in, and fluobenzene is formed according to the equation



On account of the volatility of the fluobenzene a worm condenser surrounded by a freezing mixture should be used, and the receiver should be closed with a doubly bored cork and provided with a tube bent so as to dip into a vessel of mercury. More than the above quantities must not be used.

Ekbom and Manzelius (Ber. **22**, 1,846) have recently prepared fluonaphthalene, $\text{C}_{10}\text{H}_7\text{F}$, by dissolving α - or β -naphthylamine in strong hydrofluoric acid in a platinum basin and adding the necessary amount of potassium nitrite dissolved in a little water. A good deal of tarry material is formed with the fluonaphthalene, and the latter is separated by neutralising the acid with soda, adding caustic soda to hold naphthols, and distilling in a current of steam.

3. Chromium Hexafluoride.—Jackson and Hartshorn (Ber. **18**, 1,993) prepared difluobenzoic acid by the action of chromium hexafluoride on dry benzoic acid. A black crust was formed, from which the product was extracted with soda. The hexafluoride, which is reduced to CrF_3 by the action, they prepared by distilling fuming sulphuric acid (180 gr.), potassium dichromate (60 gr.), and fluor spar (100 gr.).

CHAPTER XVII

PREPARATION OF NITRO-DERIVATIVES

1. General Remarks.—The agents used in preparing nitro-derivatives are nitric acid, fuming nitric acid, mixtures of sulphuric acid with nitric acid, alkaline nitrates and nitrate of urea, a mixture of nitric and acetic acids, silver nitrite, and potassium nitrite. A few less common methods will be mentioned in the sequel.

Substances of the aromatic series can usually be converted into nitro-derivatives by the action of nitric acid. In the case of fatty bodies this is not possible, because the acid tends rather to oxidise the substances submitted to its influence.

In regard to aromatic substances it may be said that, in general, as low a temperature must be employed as possible, as the acid has a greater tendency to oxidise the higher the temperature is. Side chains are particularly apt to be oxidised to carboxyl groups. The more numerous the side chains are, however, the easier is it to prepare nitro-derivatives. Sulphonated compounds are specially easily acted upon. It has not hitherto been found possible to introduce more than four nitro-groups into one ring.

Nitro-groups have the effect of rendering neighbouring halogen atoms much more replaceable. Thus ortho- and parachloronitrobenzene give nitraniline when they are heated with alcoholic ammonia. The meta-compound does not react. The presence of two or three nitro-groups is still more favourable to the action.

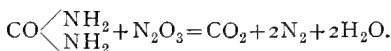
The following table, abbreviated from that of Ure, gives the content of HNO_3 in nitric acids of different densities¹ :—

¹ The use of this table in preparing acid of any required strength may be illustrated as follows: If the problem is to convert acid of sp. gr. 1.476,

Table of Specific Gravity of Nitric Acid at 16.5°.

Sp. Gr.	HNO ₃ .	Sp. Gr.	HNO ₃ .	Sp. Gr.	HNO ₃ .
1.500 .	93.0	1.383 . .	62.3	1.196 .	31.6
1.498 .	92.0	1.368 . .	59.6	1.183 .	29.7
1.494 .	90.2	1.358 .	57.6	1.171 . .	27.9
1.488 .	88.3	1.348 . .	55.9	1.159 .	26.0
1.482 .	86.4	1.338 .	53.9	1.146 .	24.1
1.476 .	84.6	1.322 .	51.1	1.134 .	22.3
1.470 .	82.7	1.311 .	49.2	1.123 . .	20.4
1.464 .	80.9	1.300 .	47.1	1.111 .	18.5
1.453 .	78.0	1.289 .	45.5	1.099 . .	16.7
1.446 .	76.2	1.276 .	43.7	1.088 . .	14.8
1.439 .	74.4	1.258 .	40.9	1.076 .	13.1
1.431 .	72.6	1.246 .	39.1	1.059 .	10.2
1.423 .	70.7	1.234 .	37.2	1.048 .	8.4
1.415 .	68.8	1.221 .	35.3	1.037 .	6.5
1.406 .	66.9	1.208 .	33.5	1.027 .	4.7
1.394 .	64.1				

To obtain nitric acid free from nitrous acid, 6 grams of urea are added to each litre of the nitric acid (sp. gr. 1.40). The acid is then heated to boiling, and a rapid current of air is driven through it for a few seconds. The action of the urea was explained by Millon (Ann. Ch. Ph. [3], 6, 37).



In preparing nitro-derivatives of aromatic acids, salts of the acids may be used to start from.

2. Method of using Nitric Acid.—Ordinary or fuming nitric acid is simply poured on to the substance, if it is a liquid. If it

containing therefore 84.6 per cent. HNO₃, to acid of sp. gr. 1.208, containing 33.5 per cent. of HNO₃, we divide the former percentage by the latter and obtain the quotient 2.52. This tells us that 100 parts of the concentrated acid and 152 parts of water will give us 252 parts of acid of the required strength.

If, on the other hand, the question is to prepare 500 grams of acid of sp. gr. 1.208 from acid of sp. gr. 1.476, we calculate as follows :

$$\frac{500 \times 33.5}{84.6} = 198.$$

This tells us that 198 grams of the concentrated acid with 302 cc. of water will give the required amount of dilute acid.

is solid, it is either pulverised or dissolved in a little water, alcohol, ether, or acetic acid. If the action proceeds with difficulty only, the substance may be added to the nitric acid, and the latter may be warmed if necessary. In some cases the pure acid of the composition HNO_3 is used.

3. Preparation of Nitro-Derivatives of Bases.—The above method holds for almost all aromatic substances excepting amines. The amine group interacts with the acid before the nitro-body can be formed, and so nitro-amines are not produced.

This undesirable secondary action does not take place in presence of a large excess of sulphuric acid, and it can also be avoided by replacing one or both of the hydrogen atoms of the NH_2 by organic radicals. Nitric acid, in presence of sulphuric acid, forms chiefly meta-compounds while acetyl and benzoyl derivatives give chiefly ortho- and para-compounds.

Nölting and Collin (Ber. **17**, 561) have stated that in presence of sulphuric acid meta-compounds are formed exclusively. But later investigations have shown that, although the meta-compound is always the chief product, it is not invariably the only one.

Hübner (Ber. **10**, 1,706) dissolved sulphate of aniline in a large quantity of cold concentrated sulphuric acid, and added drop by drop the calculated amount of nitric acid largely diluted with sulphuric acid. Water was then added, the mixture being kept cool during the process, and the acid was neutralised with carbonate of soda. The precipitated nitranilines were separated by driving the ortho- and meta-compounds over with steam, while the para-compound remained behind, not being volatile with water vapour.

When nitric acid acts on *p*-toluidine in presence of ten parts of concentrated sulphuric acid, two nitrotoluidines, melting at 114° and 78° respectively are formed. If fifteen or twenty or more parts of sulphuric acid are taken, the nitro-compound melting at 78° is formed alone. To prepare this substance (Ber. **17**, 263) *p*-toluidine (100 gr.) is dissolved in sulphuric acid sp. gr. 1.842 (2,000 gr.) in a strong vessel. The solution is cooled by means of ice and salt to a temperature below 0° , and a mixture of nitric acid sp. gr. 1.48 (75 gr.) and sulphuric acid sp. gr. 1.84 (300 gr.) is allowed to flow into the well-stirred solution. The temperature must not be allowed to exceed 0° by more than a few degrees. The lower the temperature, the purer the product will be. When all the acid has been added

the mixture is allowed to stand for a short time and is then poured slowly into 5-6 litres of water which is cooled with ice, so that the temperature may never exceed 25° . After being filtered from impurities, this solution is diluted to 15-20 litres and neutralised with solid carbonate of soda, care being taken as before to keep the temperature as low as possible. If caustic soda is used, the temperature rises too high. The precipitate is collected on cheese cloth and pressed dry. The product is finally recrystallised from alcohol. In this way from 100 grams of toluidine at least a like amount of *m*-nitrotoluidine, melting at 78° , may be obtained.

Following a suggestion given later by Nölting and Stoecklin (Ber. **24**, 566), it is advisable to add a little urea to the solutions of the bases in sulphuric acid, to decompose any nitrous acid which may be formed. The yields are thereby improved, and the products are purer.

Groll (Ber. **19**, 198) dissolved dimethylaniline (200 gr.) in sulphuric acid of sp. gr. 1.84 (4,000 gr.) and cooled the solution in a freezing mixture. If less acid is taken, much of the material will become resinised and thus be lost. A cold mixture of nitric acid of sp. gr. 1.37 (193 gr.) and sulphuric acid of sp. gr. 1.84 (600 gr.) is then added drop by drop in such a way that the temperature does not exceed $+5^{\circ}$. After the whole has remained at rest for five hours, it is poured into ten litres of ice-water. *p*-Nitrodimehtylaniline is precipitated, and the quantity increases when soda is added, until the colour of the liquid suddenly changes to red. At this point the precipitate is filtered off. More soda is added to the filtrate, and a red substance is precipitated along with sodium sulphate. About 160-170 grams of the former, which is *m*-nitrodimehtylaniline, can be extracted from the precipitate with alcohol.

Amido-acids can be converted into nitro-derivatives (Ber. **22**, 292) by this method.

Nölting and Collin (Ber. **17**, 262) prepared *p*-nitraniline by dissolving acetanilide (1 kg.) in sulphuric acid of sp. gr. 1.84 (4 kg.) and allowing nitric acid of sp. gr. 1.478 (590 gr.) diluted with sulphuric acid (1,200 gr.) to flow in slowly. During the whole operation the vessel stood in a freezing mixture of ice and salt. On account of the difficulty in dissolving the acetanilide in sulphuric acid, it was first dissolved in a small amount of warm glacial acetic acid, and this solution, when cold, was mixed with the sulphuric acid. When this mixture was poured into water, 95 per cent. of the possible amount of nitracetanilide was precipitated. *p*-nitraniline was

obtained from it eventually by hydrolysis. A little *o*-nitraniline remains in the mother-liquors.

Hübner (Ann. **208**, 292) obtained larger quantities of the latter by the action of nitric acid on benzanilide (cf. p. 226). He added pulverised benzanilide (10 gr.) gradually to nitric acid of sp. gr. 1.45 (100 gr.) at 14°, and immediately poured the mixture into 12–14 times its bulk of cold water. A mixture of *o*-nitrobenzanilide and *p*-nitrobenzanilide was precipitated with hardly any of the meta-compound, and by boiling with caustic soda these were decomposed into sodium benzoate and the corresponding nitranilines. The latter were separated by distillation in a current of steam.

Mertens (Ber. **10** 995) prepared dinitrodimethylaniline by dissolving dimethylaniline (10 parts) in nitric acid (110 parts) and water (110 parts), and allowing the mixture to stand for six hours.

4. Nitro-Derivatives of Easily Oxidisable Substances.—Substances which, like quinol, are easily oxidised, cannot be treated directly with nitric acid. Nietzki (Ann. **215** 142) first converted it into diacetylquinol, and then dissolved the acetyl derivative in 5–6 times as much nitric acid of sp. gr. 1.5. The acid was cooled so as to keep the temperature below 10°. After allowing the solution to remain in the freezing mixture for several hours, it was poured into ice-water and the dinitrodiacetylhydroquinone precipitated. The acetyl groups were removed by the action of cold caustic potash.

Similarly gallic acid (trioxybenzoic acid) would be oxidised by nitric acid to oxalic acid, but the triethyl ether can be easily converted into nitropyrogallol triethyl ether, carbon dioxide being lost in the process (Schiffer, Ber. **25**, 722).

If care is taken, nitroaldehydes can be prepared from aldehydes without any acid being formed. Thus when nitric acid acts at a low temperature and for a short time on *m*-oxybenzaldehyde,¹ nitro-*m*-oxybenzaldehyde is formed.

Erdmann dissolved *p*-chlorobenzaldehyde in six parts of sulphuric acid and treated it, at a temperature not exceeding 25°, with 78 per cent. nitric acid. The yield of *p*-chloro-*m*-nitrobenzaldehyde was quantitative. In this substance the chlorine atom is very easily replaced. In a later communication he recommends heating the mixture for a quarter of an hour at 80–90° before pouring it into water.

¹ Ber. **22** 2,348. Cf. Ber. **9**, 1463, and **13**, 310.

When the substances are very sensitive still lower temperatures than these must be used. Thus comparatively few nitropyrrol derivatives are known because they are unable to withstand the action of the nitric acid. Ciamician and Silber (Ber. **18**, 1,456) found that pyrrolmethylketone was entirely decomposed by nitric acid at the ordinary temperature, but by taking only 5 grams at a time and dissolving it in fuming nitric acid cooled to -18° , and then pouring the solution into ice-water, they obtained nitropyrrolmethylketone. Three other nitro-derivatives were formed at the same time.

5. Other Special Cases.—In preparing nitrophenanthrene Schmidt (Ber. **12**, 1,154) proceeded as follows: He tried first nitric acid of sp. gr. 1.5 at -10° and acid of sp. gr. 1.35 at the ordinary temperature, but in both cases obtained much resinous matter and very little of the desired product. Finally, he mixed phenanthrene (1 part) with coarse sand ($3\frac{1}{2}$ parts), which had previously been washed with nitric acid, and stirred the mixture thoroughly with nitric acid of sp. gr. 1.35 (8 parts). The object of the addition of sand was to enable the acid to reach every part of the phenanthrene and prevent its collecting in a tough sticky mass. The whole was left to itself for three or four days at 10° . On washing away the acid and extracting the residue with 90 per cent. alcohol, about 49 per cent. of the phenanthrene was recovered as mononitrophenanthrene.

In trying to prepare trinitronaphthol, Martius (Z. Ch. **1868**, 82) found that dinitronaphthol could be dissolved in cold nitric acid without decomposition, but that on boiling the solution the substance was broken down into phthalic acid and oxalic acid. So that naphthopicric acid could not be obtained in this way. Later, Eckstrand (Ber. **11**, 162) succeeded in preparing it (cf. § 12) by adding dinitronaphthol to four times its weight of a mixture of equal parts of fuming and ordinary nitric acid, and, with frequent stirring, warming the solution for several hours in a water bath at $40-50^{\circ}$, care being taken that the temperature did not exceed these limits. Although the whole of the substance had not even finally gone into solution, the mixture was poured into water. The precipitate consisted of a mixture of the unchanged substance with trinitronaphthol. These were separated by recrystallisation. The yield was 20 per cent. of the theoretical.

Mono- and dinitrothiophene were obtained by Meyer and Städler (Ber. **17**, 2,648), by passing the thiophene in a current of air through red fuming nitric acid.

6. Influence of Time and Temperature.—To illustrate the influence of these factors on the result of the action of nitric acid, some experiments of Wehr's (Dissert. Freiburg, 1891) may be mentioned. He found that *p*-tolylacetic acid (2 gr.) was not attacked after standing for twelve hours with fuming nitric acid (10 gr.). When the mixture was evaporated on the water bath, mono- and dinitro-derivatives were formed. When the same quantity was dissolved in glacial acetic acid (10 gr.) and warmed with nitric acid of sp. gr. 1.52 (10 gr.) on the water bath *m-m*-dinitro-*p*-tolylacetic acid was obtained. Taking the same quantities of the substance and of fuming nitric acid, and allowing them to remain together for three weeks at the ordinary temperature, he found as chief product mononitrotolylacetic acid. Under the same conditions the same amount of the substance with fuming nitric acid (5 gr.) and concentrated sulphuric acid (10 gr.) gave dinitrotolylacetic acid. Finally, to avoid all possibility of oxidation, fuming nitric acid (5 gr.) was mixed with pure sulphuric acid, H_2SO_4 (10 gr.), and cooled to -10° . The tollylacetic acid (3 gr.) was added cautiously so that the temperature remained below $+10^\circ$. Under these circumstances, *m-m*-dinitro-*p*-tolylacetic acid was formed.

Bauer (Ber. **24**, 2,835) found that when a solution of butyltoluene in glacial acetic acid was slowly mixed with fuming nitric acid, an oil was formed which could be driven over with steam and consisted of mononitrobutyltoluene. But when the hydrocarbon itself was allowed to drop into strongly cooled fuming nitric acid, and the mixture was set aside at the ordinary temperature, the mono-, di-, and trinitro-derivatives were produced. Trinitrobutyltoluene, artificial musk, is obtained by allowing the hydrocarbon to flow slowly into five times its weight of a cold mixture of nitric acid of sp. gr. 1.5 (1 part) and fuming sulphuric acid containing 15 per cent. of anhydride (2 parts), and warming the whole on the water bath for 8–9 hours. On pouring the product into water the substance which is precipitated is not yet fully converted into the trinitro-compound. To achieve this the material must be collected, dried, and passed through the same process a second time.

Nietzki and Rösel (Ber. **23**, 3,216) obtained tetramidotoluene. They started from *m*-toluylenediamine. This they mixed with 20 per cent. of nitrate of urea and added to nitric acid distilled over sulphuric acid, keeping the temperature between 5° and 10° . This gave dinitrodiamidotoluene along with a little of the mononitro-derivative. The former gave the required substance on reduction.

7. Use of Nitric Acid containing 100 per cent. HNO_3 .—Nietzki and Hagenbach's work (Ber. **20**, 333) shows that pure HNO_3 is required for preparing many nitro-compounds. Thus they found that the action of nitric and sulphuric acids and of fuming nitric acid of sp. gr. 1.52 simply converted diacetyl-*m*-phenylenediamine into the mononitro-derivative. Dinitrodiacetylphenylenediamine required the use of nitric acid containing 100 per cent. of HNO_3 for its formation. This acid is best prepared by distilling fuming nitric acid with twice its weight of sulphuric acid. Its sp. gr. at 15° is 1.533.

According to L. Meyer (Ber. **22**, 23), however, the only way to obtain nitric acid perfectly free from water, is to add nitric anhydride in excess to the acid got by distillation over sulphuric acid, determine the excess of the anhydride by titration, and add the amount of more dilute acid shown by the analysis to be required.

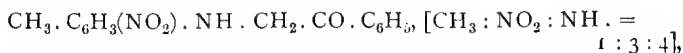
Meyer (J. pr. Ch. **114**, 342) prepared the anhydride by distilling almost anhydrous nitric acid over phosphorus pentoxide. Very little heat is giving out on mixing the ingredients.

The action of nitric anhydride itself is much more violent than that of the strongest nitric acid, but the products are the same in both cases.

8. Action of Dilute Nitric Acid.—The investigations of Norton and Allen (Ber. **18**, 1,995) show that the general impression, that dilute nitric acid usually acts as an oxidising agent towards organic bodies, is incorrect. As early as 1859 Fritzsche (Ann. **110**, 151) had shown that when phenol (2 parts) is dissolved in warm water (100 parts) and fuming nitric acid (3 parts) is added, a large amount of nitrophenol is obtained. But this remained an isolated statement. Norton and Allen used nitric acid of sp. gr. 1.029, which contained therefore only about 4 per cent. of the acid. On boiling 1 gram of methylacetanilide in 100 cc. of this for two hours, dinitromethylaniline was deposited when the solution cooled. Even when acid of only half the above strength was taken the same compound was formed with somewhat greater difficulty. Dinitroethylacetanilide was prepared in the same way. Phenylacetanilide gave trinitrodiphenylamine. To obtain the same substance from phenylbenzanilide the boiling had to be continued for several days. Even then a good deal of unchanged substance was recovered. It is probable that the more easily the acid radical is removable from the anilide, the easier it is to form the nitro-compound.

Lellmann and Donner (Ber. **23**, 169) tested the action of nitric

acid on phenacyltoluidine. They found that a 22 per cent. acid gave the mononitro-compound—



while a 65 per cent. acid introduced two nitro-groups.

9. Action of Nitric Acid on Fatty Bodies.—The resemblance of fatty tertiary alcohols to the phenols might render the formation of nitro-derivatives of this class of substances not unexpected. In both classes the group : COH is connected with carbon only. In order that oxidation may take place the molecule must be broken up, a circumstance which would therefore favour the other possibility. Taking these things into consideration Haitinger (Ann. **193**, 368), at the instigation of Lieben, examined the action of nitric acid on tertiary butyl alcohol, $\begin{matrix} \text{CH}_3 \\ \diagup \\ \text{C} \\ \diagdown \\ \text{CH}_3 \end{matrix} \begin{matrix} \text{CH}_3 \\ \diagdown \\ \text{C} \\ \diagup \\ \text{OH} \end{matrix}$. By running the alcohol gradually into the cooled nitric acid, the method which experience showed to be the best, he obtained nitrobutylene as an oil, which was dried with anhydrous calcium nitrate. The yield was 8–10 per cent. of the alcohol used. In another paper (M. f. Ch. **2**, 286), he describes the preparation of the same substance by leading isobutylene gas in a slow stream into an absorption tower. Nitric acid is allowed to trickle through the latter at such a rate that the liquid flowing out at the foot is green in colour. Hardly any nitroethylene can be made by this method.

10. Use of Ether as a Solvent.—This solvent was used by Benedikt (M. f. Ch. **3**, 386). He dissolved pyrocatechin (10 gr.) in ether (500 cc.) and added fuming nitric acid (4 cc.). After the substances had remained in contact for twenty-four hours, mononitropyrocatechin was found in the ether. When eugenol was treated in the same way the yield of nitroeugenol was almost quantitative. The product was extracted by adding alcoholic caustic potash to the reddish-brown liquid until all the nitric acid was precipitated as potassium nitrate. This was removed by filtration, and the addition of caustic potash was continued as long as the red precipitate of nitroeugenol-potassium increased in quantity. The salt was finally dissolved in water and decomposed with sulphuric acid.

11. Use of Acetic Acid as a Solvent.—The use of acetic acid has already been mentioned. It seems to be very valuable in many cases, because in its presence the calculated amount only of nitric acid need be taken. Thus Cosak (Ber. **13**, 1,088) dissolved *p*-acettoluide (10 gr.) in glacial acetic acid (45 gr.) and added the calculated amount of nitric acid of sp. gr. 1.47 (37 gr.). In such a case the formation of a dinitro-derivative is almost an impossibility, since the nitric acid is not present in excess, and besides its action is weakened by the acetic acid.

Städel and Kolb (Ann. **259**, 210) mixed *m*-cresol (140 gr.) with glacial acetic acid (140 gr.), cooled the mixture to -5° , and allowed a slow stream of a solution of nitric acid of sp. gr. 1.5 (200 gr.) in acetic acid (400 gr.) cooled to -15° to flow into it. During the hour and a half that this operation lasted the temperature never rose above -1° . The reddish-brown liquid was then poured into a kilogram of ice, and water (1½ kg.) was added. After the lapse of twelve hours, the crystals were collected on a filter, and the filtrate was extracted with ether. The crystals left on evaporation of the latter were distilled with steam. 39 + 12 grams of volatile, and 47 + 18 grams of non-volatile, nitro-*m*-cresol were obtained.

12. Use of Mixture of Nitric and Sulphuric Acids.—This mixture is used even more frequently than that with acetic acid. The constituents of the acid used by Schönbein (Pogg. Ann. **70**, 320), in 1846, for preparing gun cotton were concentrated sulphuric acid of sp. gr. 1.846 and nitric acid of sp. gr. 1.385–1.440. According to Friedländer,¹ it has entirely taken the place of the expensive fuming nitric acid in manufacturing operations, on account of the inconveniences attending the employment of the latter and the fact that the powerful attraction of sulphuric acid for water permits the use of little more than the theoretical amount of nitric acid, and none is wasted.

The mixture is used in the same way as nitric acid itself. The nitro-compounds of benzene, toluene, and xylene are prepared in the cold, while in the case of naphthalene a temperature of 40 – 50° is required. Dinitrobenzene is formed when the mixture acts on nitrobenzene in the heat.

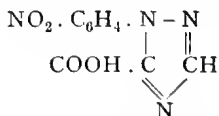
According to Armstrong and Rossiter (Proc. Ch. Soc. **1891**, 87–89; Ber. **24**, 721c), the sulphuric acid, besides keeping up

¹ Fortschritte der Teerfarbenfabrikation, 3

the concentration of the nitric acid, has also an influence in directing the course of the action.

In laboratories the proportions of the acids used frequently vary from those used in chemical works. Thus Schultz (Ann. **174**, 221) placed diphenyl (3 gr.) in a flask, and covered it with nitric acid of sp. gr. 1.45 (6 gr.) and sulphuric acid (1 gr.). The action was completed by boiling the mixture, which, on cooling, deposited a mass of crystals, consisting of dinitrodiphenyl entirely free from its isomers. The crystals were collected on a filter, washed with water, and boiled several times with alcohol.

Bladin (Ber. **25**, 742) boiled phenyltriazole carboxylic acid (10 gr.) with fuming nitric acid (100 gr.) and sulphuric acid (50 gr.) for eight or ten minutes. On pouring the liquid into ice-water, nitrophenyltriazole carboxylic acid (11.5 gr.) was obtained—



The addition of fuming sulphuric acid in preparing artificial musk has already been mentioned (§ 6).

Here, as usual, temperature has an important influence on the course of the action and on the yield.

In preparing nitro-derivatives of azoxybenzene, Klinger and Zuurdeeg (Ann. **255**, 319) found that when the substance (20 gr.) was covered with nitric acid of sp. gr. 1.50 (200 gr.) and sulphuric acid of sp. gr. 1.80 (100 gr.) and the mixture was immediately poured into water, the product was extremely resinous. But when the ingredients were cooled during the operation, the trinitroazoxybenzene separated out free from resinous matter in the course of twenty-four hours. From 60 grams of azoxybenzene, with the temperature at -20° , they got 55 grams of the crude product. With the temperature at -10° , they got only 35 grams; while working at $+10^\circ$, nothing separated from the mixture at all.

Trinitronaphthol (cf. § 5) was prepared by Diehl and Merz (Ber. **11**, 1,661), as follows: They mixed finely pulverized dinitronaphthol with excess of sulphuric acid, cooled the mixture, and added a solution of fuming nitric acid in sulphuric acid. After the liquid had remained at rest for some time it was poured into ice-water. The most of the precipitate was trinitronaphthol. They tried to improve the yield by varying the proportions of the acids.

Finally, they found that dinitronaphthol (100 gr.) with nitric acid (25 cc.) and sulphuric acid (1,500 gr.), after standing for ten days, gave 83·9 per cent. of the theoretical yield of the product. The mass stood for that length of time in cold water, and was stirred periodically, a point which seemed to be of material importance.

The use of nitric acid or of the mixture may make a great difference in the relative amounts of the various isomers obtained. Thus, according to Nölting (Ber. **18**, 2,672), toluene gives with nitric acid alone chiefly *p*-nitrotoluene (66 per cent.), while with the mixed acids it gives chiefly the ortho-compound (60–66 per cent.). Probably the temperature and strength of the acids likewise make a difference in the proportions of the isomers formed. These facts are of great importance from a technical point of view. Baeyer's synthesis of indigo, for example, cannot be employed on economical grounds, because in preparing the orthonitrocinnamic ether so much of the comparatively valueless para-compound is formed at the same time (Caro, Ber. **25**, 987*c*).

13. Use of Sodium and Potassium Nitrates.—Many substances which yield nitro-compounds with difficulty can be successfully treated by adding first sulphuric acid and then saltpetre or *vice versa*. This method used to be a favourite one. For example, Gerland (Ann. **91**, 187) prepared nitrobenzoic acid by mixing benzoic acid with twice its weight of saltpetre and adding an equal quantity of concentrated sulphuric acid. The yield is stated to be good. The method seems recently to have recovered its popularity.

The preparation of *p*-nitro-*m*-chlorobenzaldehyde by Erdmann has already been mentioned. Eichengrün and Einhorn (Ann. **262**, 136) obtained the orthonitro-compound by cooling a solution of sodium nitrate (11 gr.) in sulphuric acid (200 gr.) and adding drop by drop *m*-chlorobenzaldehyde (15 gr.) from a pipette with a capillary opening, and continuously stirring the solution during the addition. It is best to keep the temperature below 0°. When the mixture is poured into ice, some hours after the completion of the action, the compound is deposited in crystalline form.

Täuber (Ber. **23**, 795) dissolved pure benzidine sulphate (28·2 gr. = $\frac{1}{10}$ mol.) in sulphuric acid (300 gr.), warming the mixture slightly to facilitate the solution, and then cooling it to 10–20°. This temperature is not low enough to cause a re-deposit of the sulphate. He then added gradually potassium nitrate (20·2 gr. = $\frac{3}{10}$ mol.), stirred the mixture for several hours, and then poured it into three times its weight of water. A

small amount of a yellow precipitate is removed by filtration, and the *m*-dinitrobenzidine is precipitated from the filtrate with soda.

When oxyazobenzenesulphonic acid is dissolved in concentrated sulphuric acid of sp. gr. 1.842 at 10–20°, potassium nitrate is added to the well-stirred solution, the stirring being continued for two hours, and the mixture is finally poured into water, a quantitative yield of nitroxyazobenzenesulphonic acid is obtained.

Seitz (Ber. **22**, 257) prepared a dinitro-compound of β -naphthoquinaldine by mixing the dry nitric acid salt of the base with concentrated sulphuric acid.

When the substance is acted on by nitric acid with difficulty, it may be dissolved in sulphuric acid and the solution heated to 100° before the calculated amount of potassium nitrate is added.

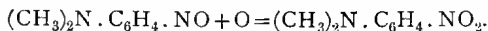
14. Separation of Nitro-Compounds from Acid Solutions in which they are formed. A few general remarks on this subject may not be out of place here. Cases have already been mentioned in which the compounds crystallise out directly. In others, we have seen, the product separates when the solution is poured into water. When neither of these methods is successful, the nitro-compounds can be extracted from the solution in water by means of ether. To avoid this labour, or in cases where the extraction cannot be carried out, the nitric acid can be cautiously evaporated on the water bath, alcohol being added from time to time to prevent the acid becoming too concentrated, or else the acid may be neutralised with sodium carbonate before the evaporation begins, and the dry residue may then be extracted with alcohol, ether, or other suitable medium.

When Suida and Plohn (M. f. Ch. **1**, 182) prepared nitroethylphenol by addition of fuming nitric acid to ethylphenol and dilution with water, most of the product was at once precipitated. The portion which remained dissolved was obtained by neutralising with ammonia and precipitating with lead acetate. The insoluble salt was very explosive and was decomposed by addition of acid to the moist compound.

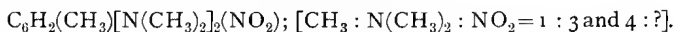
15. Less Common Methods of Preparing Nitro-Compounds.—A very generally applicable method is to dissolve the substance in glacial acetic acid and conduct into the solution the *gases* given off on heating *lead nitrate*.

The oxidation of *nitroso-bodies* also gives nitro-compounds. Thus Schraube (Ber. **8**, 620) treated nitrosodimethylaniline with alkaline

solutions of potassium ferricyanide and of potassium permanganate. He prepared nitrodimethylaniline in both those ways, and extracted it from the solution with ether. As the product can only be extracted with difficulty by ether, Wurster (Ber. **12**, 529), who repeated the experiments with permanganate, recommended the evaporation of the mass to dryness and extraction of the residue with benzene—



Sodium nitrite in acid solution has likewise the power of producing nitro-derivatives. For example, Niementowsky (Ber. **20**, 1,890) dissolved tetramethyldiamidotoluene in glacial acetic acid, and added a solution of sodium nitrite as long as any fresh turbidity appeared. When the precipitate had been recrystallised from petroleum ether it was found to be, not the expected nitrosamine, but mononitrotetramethyldiamidotoluene—



Deninger (J. pr. Ch. **148**, 298) likewise succeeded in preparing nitro-compounds from amines and phenols by means of nascent nitrous acid. Of course, the amines are converted through the diazo-stage into phenols by this process.

The yields, which are often very good, depend on the conditions of experiment. In the case of aniline (10 gr.), the substance is dissolved in concentrated sulphuric acid (20 cc.) and water (80 cc.), and the solution is cooled to 15°. Commercial sodium nitrite (300 gr.) dissolved in water (100 cc.) is then added. During the addition of the first third of the nitrite the solution is cooled, the remainder is then poured in rapidly without cooling. The mixture is then placed in a large vessel on a water bath and boiling dilute sulphuric acid (1:1) is added as rapidly as the violent action will permit. When the interaction is over, the ortho-compound can be driven over with steam. The para-compound is isolated from the residue by recrystallisation from water or hydrochloric acid. The yield is 4·7 grams ortho- and 3·3 grams paranitrophenol.

When substances are employed in which the para-position is occupied, the yield is almost quantitative. Thus 50 grams of toluidine give 70 grams of dinitrodisresol.

When salicylic acid (1 mol.) is suspended in water and sodium nitrite (2 mol.) is added, the acid goes gradually into solution. On mixing this solution with sulphuric acid until the temperature has reached 60°, heating the mixture on the water bath till nitrous fumes cease to be evolved, and then allowing the mass to cool, a

deposit of salicylic acid and asymmetrical nitrosalicylic acid is formed. The yield of the latter is 80 per cent. By working in glacial acetic acid solution the yield is improved; 10 grams of salicylic acid give 11 grams of the nitro-acid.

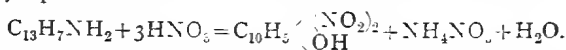
In a later communication Deninger (J. pr. Ch. **150**, 550) states that, while nitric acid gives rise almost exclusively to the asymmetrical nitrosalicylic acid melting at 228° , and yields but little of the isomer melting at 144° , his process permits of the preparation of either of these substances, the yield being in each case better than by any previously known method. His method likewise gives a 90 per cent. yield of nitro-*p*-oxybenzoic acid [$\text{COOH} : \text{NO}_2 : \text{OH} = 1 : 3 : 4$]. To obtain asymmetrical *m*-nitrosalicylic acid [$\text{COOH} : \text{OH} : \text{NO}_2 = 1 : 2 : 5$], salicylic acid (100 gr.) and sodium nitrite (130 gr.) are mixed with water (150 cc.), and sulphuric acid of sp. gr. 1.52 (1,200 cc.) is slowly added. The temperature of the acid must not exceed 15° . After a lapse of four hours the mixture is warmed to 50° , and allowed to stand until nitrous fumes cease to be evolved. Finally, the mass is warmed on the water bath. The crystals which separate on cooling are collected on a filter, washed, and recrystallised twice from water. The yield is 85 grams.

The *m*-nitrosalicylic acid [$\text{COOH} : \text{OH} : \text{NO}_2 = 1 : 2 : 3$] is obtained by mixing salicylic acid (100 gr.), sodium nitrite (170 gr.), and water (150 cc.), and adding rapidly warm (60°) sulphuric acid of sp. gr. 1.52 (1 l.). As the action is very violent, a large vessel, which stands from the beginning on the water bath, must be taken. If the mass does not become red by this treatment an extra 100 cc. of sulphuric acid must be added. The material which separates on cooling is removed by filtration and boiled for some time with animal charcoal. The nitrophenol which is always formed is removed by this process. A second crystallisation from water gives 70–80 grams of the required isomer, melting at 144° .

Goldschmidt (M. f. Ch. **2**, 250) attempted to obtain isomers of already known nitropyrenes by superposing an ethereal solution of the pure hydrocarbon on a moderately concentrated solution of *potassium nitrite* in water, and adding sulphuric acid slowly through a dropping funnel. An already known dinitropyrene along with a small amount of a mononitro-compound were the only products however.

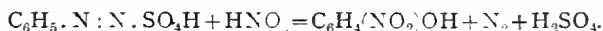
In the course of his researches on *diazo-bodies*, Griess showed that they give dinitrophenols on being *warmed with nitric acid*. This explains the fact that when amines are heated with nitric acid

they give dinitrophenols. This action was first noticed by Ballo (Z. Ch. **1870**, 51), who obtained dinitronaphthol by mixing naphthylamine and nitric acid, and allowing them to become warm spontaneously. He explained this at the time by giving the extraordinary equation—



The yield by this method is so good in this particular case that it is said to be still in use for technical purposes.

Nölting and Wild (Ber. **18**, 1338) tried successfully to prepare mononitrophenols by the action of one molecular proportion of nitric acid on diazo-bodies. Thus they converted aniline into nitrophenol. Aniline (93 gr.) was dissolved in concentrated sulphuric acid (150 to 200 gr.) and water (2 l.), and the solution having been cooled with ice, sodium nitrite (69 gr.) was added. After the lapse of a short time nitric acid of sp. gr. 1.335 (119 gr. = 63 gr. HNO_3) was added, and the whole was heated in a flask attached to a reflux condenser until the evolution of nitrogen had ceased. The *o*-nitrophenol was then distilled off with steam, and the *p*-nitrophenol which remained behind was purified by recrystallisation from water. An excellent yield, consisting of almost equal quantities of the isomers, was obtained. The action is represented by the equation—



Paratoluidine, *o*-toluidine and naphthylamine gave good, moderately good, and rather poor yields respectively.

Fittica (J. pr. Ch. **125**, 189) obtained a fourth nitrobenzoic acid by dissolving benzoic acid (1 mol.) in absolute ether, adding *ethyl nitrate* (1 mol.), and allowing this mixture to flow drop by drop into concentrated sulphuric acid. Quantities of nitrobenzoic ether and other products were formed. He prepared also in the same way a nitrobenzaldehyde corresponding to this acid.

Sandmeyer's method (Ber. **20**, 1,494) enables us to replace aromatic amine groups by nitro-groups. Aniline (9 gr.), water (50 cc.), and nitric acid of sp. gr. 1.4 (20 gr.) are mixed, and to the cooled solution sodium nitrite (15 gr.) dissolved in water (50 cc.) is added. This mixture is poured slowly into a flask containing the solution of cuprous salt, and the mass is allowed to remain for an hour during the evolution of the nitrogen. Nitrobenzene (5 gr.) was finally isolated by distillation.

The solution of cuprous salt for such purposes is prepared as follows: Crystallised cupric sulphate (50 grams) (2 mol.) and ordinary grape sugar (15 grams) are dissolved in 100 cc. of warm water, and to the boiling liquid a cold solution of 20 grams of caustic soda in 60 cc. of water is added. The mixture is shaken until all the copper has been reduced to the cuprous state, and then the mass is rapidly cooled. The excess of caustic soda is finally neutralised by the addition of an equivalent amount, or slight excess, of acetic acid.

It may be mentioned in closing this paragraph that Ihrfeld (Ber. **22**, 692*c*) found that benzenesulphonamidoacetic acid, $\text{C}_6\text{H}_5 \cdot \text{SO}_2 \cdot \text{NH} \cdot \text{CH}_2 \cdot \text{COOH}$, with fuming nitric acid gave a nitroso-derivative, $\text{C}_6\text{H}_5 \cdot \text{SO}_2 \cdot \text{N}(\text{NO}) \cdot \text{CH}_2 \cdot \text{COOH}$, instead of a nitro-compound.

16. Nitro-Compounds of the Fatty Series.—As we have already stated, nitro-compounds of the fatty series can be obtained by the use of silver nitrite only, although Kolbe (J. pr. Ch. **113**, 427) has shown that its place can sometimes be taken by potassium nitrite. The method was discovered by V. Meyer (Ann. **171**, 18), and the few compounds of this class known before his work began are mentioned in the first page of his paper.

To prepare the silver nitrite, he recommends mixing lukewarm concentrated solutions of silver nitrate (2,400 gr.) and potassium nitrite (1,500 gr.), and allowing the mixture to cool. The precipitate of silver nitrite is then collected on a filter and rapidly washed.

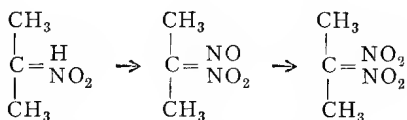
In making nitroethane he places the silver nitrite (2,090 gr.) in a large round-bottomed flask, closed by a cork provided with two holes. A long wide condenser passes vertically through one of the openings. A funnel to hold the ethyl iodide, provided with a stop-cock, passes through the other. In this work silver and iodine cannot be replaced by cheaper materials. A trial with lead nitrite was unsuccessful, and ethyl bromide, chloracetic acid, and ethylene bromide were found to be without action on silver nitrite even at the boiling temperature.

The ethyl iodide (1,700 gr.) is then allowed to flow into the flask. During this process the flask is not disturbed, as it is important that the silver nitrite should be gradually penetrated by the iodide. The iodide is admitted at such a rate that the liquid boils vigorously, but not too violently. The mass is finally warmed for some time on the water bath. When this method is pursued, the annoying aggregation of the silver nitrite into lumps is avoided, and admix-

ture with sand to prevent this is rendered unnecessary. The presence of sand interferes greatly with the recovery of the silver, causing frothing over of the mass when the iodide is fused with soda. The nitroethane is isolated by fractional distillation. The yield is about 50 per cent., and it appears that approximately equal amounts of nitroethane and ethyl nitrite are found.

The reaction failed in the cases of allyl iodide, methylene iodide, and similar substances. Oils containing nitrogen were formed which could not be purified. Twenty years later Meyer found that these oils gave pure sodium salts of nitrohydrocarbons on addition of sodium ethylate. He continued the experimental investigation in association with Askenasy (Ber. **25**, 1,701). They dissolved allyl iodide in two or three times its bulk of ether, and then treated it with silver nitrite. The almost colourless solution of the product was filtered from the precipitate, and the latter was extracted with ether. After standing for six hours the solution deposited some more silver iodide. It was filtered again, and twice its volume of absolute alcohol and then sodium ethylate were added. The precipitate was dried on clay plates, and the nitropropylene was set free by dissolving it in water, adding the calculated amount of dilute sulphuric acid and extracting with ether.¹

The preparation of dinitro-compounds could only be achieved indirectly. Thus Meyer and Locher (Ber. **7**, 1,617) prepared propyl pseudonitrole by the action of nitrous acid on secondary nitropropane, and by oxidising the former with chromic acid obtained dinitropropane.

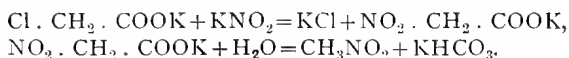


Forcrand (C. R. **88**, 974) obtained nitroacetic ether by the action of silver nitrite on bromacetic ether, but could not purify it on account of the tendency of the liquid to decompose.

At the suggestion of Kolbe, Preibisch (J. pr. Ch. **116**, 316) experimented on the action of potassium nitrite (3 parts) on chloracetate of potassium (1 part). The concentration of the solutions seems to have no influence on the yield, but to avoid violent foaming it is

¹ In regard to the constitution of fatty nitro-compounds cf. Nef. Ann. **280** 263.

best to use dilute solutions. When 100 grams of chloracetic acid are used, the yield of nitromethane is one-half of the theoretical, with larger amounts only one-third. The nitroacetic acid is very unstable, and changes immediately into nitromethane with loss of carbon dioxide—



Bewad (Ber. **24**, 973) succeeded in preparing tertiary nitrohydrocarbons of the fatty series by a very complicated process. Villiers (C. R. **94**, 1,122) made tetranitroethylene bromide by the action of fuming nitric acid on an equal volume of ethylene bromide, but the isolation of the product presented great difficulties. Losanitsch (Ber. **15**, 472, and **16**, 2,731), by the action of concentrated nitric acid on tribromoaniline, obtained a product by the disruption of the aromatic ring, which turned out to be dibromodinitromethane.

CHAPTER XVIII

OXIDATION

1. Oxidising Agents.—The following substances are used as oxidising agents. They will be discussed in alphabetical order.

Air.	Mercuric nitrate.
Arsenic acid.	Mercuric oxide.
Azobenzene.	Nitrobenzene.
Barium peroxide.	Nitric acid.
Bleaching powder.	Nitrous acid.
Bromine.	Oxygen.
Chloranil.	Ozone.
Chloric acid.	Platinum tetrachloride.
Chloride of iodine.	Potassium bichromate.
Chlorine.	Potassium chlorate.
Chromic acid.	Potassium ferricyanide.
Chromyl chloride.	Potassium hydroxide.
Copper solution—alkaline.	Potassium iodate.
Cupric acetate.	Potassium manganate.
Cupric oxide and hydroxide.	Potassium permanganate.
Cupric sulphate.	Soda-lime.
Ferric chloride.	Sodium bichromate.
Ferric hydroxide.	Sodium nitrite.
Hydrogen peroxide.	Sodium peroxide.
Hydroxylamine.	Silver acetate.
Internal oxidation.	Silver nitrate.
Lead monoxide.	Silver oxide.
Lead peroxide.	Sulphuric acid.
Manganese dioxide.	Tin tetrachloride.
Mercuric acetate.	Zinc permanganate.
Mercuric chloride.	

2. General Remarks.—The very large number of substances which has been used for the oxidation of organic bodies illustrates the diversity of effects to be produced, and makes it easy to understand that the products may vary considerably with change in the agents employed. Lieben (Ber. **8**, 1,020) was probably the first to examine this question. At his suggestion Reichardt investigated the action of different agents on soluble starch. He found that potassium permanganate in neutral, alkaline and acid solutions, as also chromic acid, act upon it energetically, but all alike give rise to dirty brown, unpleasant products. Experiments with chlorine and alkaline copper solution gave no better results. On the other hand, by warming the solution of starch with bromine, and afterwards treating the product with silver oxide, gluconic acid was obtained. Nitric acid in the heat gave carbon dioxide and oxalic acid. Fuming nitric acid gave a mononitro-derivative of starch.

With manganese dioxide and sulphuric acid, aniline gives ammonia and very little quinone. Chromic acid mixture gives a quantitative yield of the latter. Potassium permanganate in alkaline solution gives azobenzene, ammonia, and oxalic acid. In acid solution it gives aniline-black, which, with more energetic oxidation, is converted into quinone. In neutral solution, nitrobenzene and azobenzene are the chief products. Boiling bleaching powder solution likewise gives nitrobenzene. Hydrogen peroxide in presence of weak acids gives ammonia and dianilidobenzoquinoneanilide. In presence of strong acids it seems to give an induline derivative.

Schmiedeberg and Harnack (A. Path. Pharm. **6**, 101) state that efforts to oxidise choline with permanganate and with chromic acid led to negative results. But when concentrated nitric acid was used, muscarine was easily obtained.

It has long been known that *m*-xylene, $C_6H_4(CH_3)_2$, is not attacked by dilute nitric acid, but that chromic acid mixture converts it into isophthalic acid, $C_6H_4(COOH)_2$. Paraxylene, however, is oxidised by the former to *p*-toluic acid, $C_6H_4(CH_3)COOH$, and by the latter to terephthalic acid, $C_6H_4(COOH)_2$. And finally methyl groups, which stand in the ortho-position towards halogen atoms, are only attacked very slowly and with extreme difficulty by acid oxidising agents (Ber. **24**, 3,778).

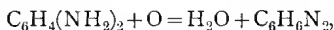
The following general statements may be useful. When the oxidation product is easily decomposed by further oxidation, it is often possible to cover the solution with a carefully chosen extracting agent, so that after each addition of the oxidising substance

the whole may be shaken and the product removed from the sphere of action of the latter. In such cases, also, the use of ice to keep the temperature as low as possible may have a favourable effect.

When the oxidised substance is volatile with steam, a current of water vapour may be conducted through the mass during the oxidation.

In many cases, where the preparation of a particular product by oxidation from another substance is found to be specially hard, it may be better to use some judiciously chosen derivative of the substance which by proper treatment will yield the same product (cf. § 8, p. 248).

3. Air.—The investigations of Bandrowsky (M. f. Ch. **10**, 124) show that not only can easily oxidisable bodies be oxidised by exposure to the air in open vessels, but that the yields obtained in this way may often be quantitative. By this method he oxidised the hydrochlorides of paraphenylenediamine and para-amidophenol in dilute solution. In the case of the first the action was represented by the equation—



and the yield almost reached the theoretically possible. The action was considerably hastened by passing oxygen through the solution or by using hydrogen peroxide.

Glaser (Ann. **154**, 150) shook the copper salt of phenylacetylene with air, in presence of alcoholic ammonia, and obtained cupric oxide and diphenyldiacetylene. This extraordinary substance has since been prepared by the action of potassium ferricyanide on cupro-phenylacetylene (cf. § 39).

Oxidation by means of air has attained increased importance since Hofmann (Ann. **145**, 358) discovered that by its means alcohols can be oxidised to aldehydes in presence of platinum. He prepared by this means the till then unknown formaldehyde, a substance which even now is obtainable in large quantities by this method alone.

On conducting the vapour of methyl alcohol in a current of air over a heated platinum spiral, he found that aldehyde was formed and could be collected by passing the products through a condenser. The apparatus was improved by Tollens (Ber. **16**, 917).

To Löw (J. pr. Ch. **141**, 323) we owe the discovery that a super-

ficially oxidised spiral of copper is more effective than platinum. In place of a solution containing at most $3\frac{1}{2}$ per cent. of the aldehyde, he obtained solutions containing 15–20 per cent. Löw found that by this method also ethers, esters, hydrocarbons, and even bases could be oxidised to aldehydes. Thus ethyl ether and acetic ether give acetic aldehyde, toluene gives benzaldehyde, and ethylamine gives acetic aldehyde and nitric oxide.

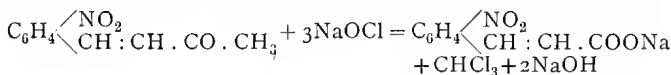
Only a few months after this, Tollens (Ber. **19**, 2,133) showed that by retaining the platinum and conducting the air through warm methyl alcohol, in an apparatus which he designed, a solution containing 30–40 per cent. of formaldehyde could be prepared by the litre with great ease.

4. Arsenic Acid.—This substance is seldom used, on account of its poisonous properties, especially as the same results can be achieved by other means. The old method of preparing fuchsine supplies an example of its application. A mixture of aniline and toluidine (Friedländer, *Farbenfabrikation*, p. 31) is mixed with one and a half parts of a syrupy solution of arsenic acid of sp. gr. 2.06, and the mixture, containing the white arseniates, is heated gradually to 180–190°.

5. Azobenzene.—Parafuchsine is prepared by heating anhydroformaldehydeaniline with five times its weight of aniline, and ten times its weight of aniline hydrochloride, using azobenzene as the oxidising agent, for three hours at 170–200°. After the excess of aniline has been driven off with steam, the residue is treated with dilute acid, and parafuchsine precipitated from the solution by the addition of salt.

6. Barium Peroxide.—This substance was employed by Lippmann (M. f. Ch. **5**, 561) for the preparation of organic peroxides. Dry hydrated barium peroxide was gradually added to benzoyl chloride, and the mixture was left at rest for two hours. The mass was then treated with water to dissolve the barium chloride. Then the benzoic acid was removed by treatment with dilute sodium carbonate. Finally, the residue was extracted three times with much boiling ether until the substance which remained burned quietly on being heated on platinum foil. In this way he obtained from 53 to 60 per cent. of the theoretical amount of benzoyl peroxide.

7. Bleaching Powder.—The action of bleaching powder as an oxidising agent corresponds closely with that of bromine in alkaline solution. It resembles this agent also in the fact that chloro-derivatives are apt to be formed (cf. § 12). According to a patent specification (Ger. Pat. 21,162), orthonitrocinnamic acid may be prepared by warming orthonitrobenzalacetone (20 parts) with a 3 per cent. solution of sodium hypochlorite (800 parts), prepared from bleaching powder and soda, until the presence of hypochlorous acid in the solution cannot be demonstrated. The yield is quantitative—



As soon as the action represented by the equation is complete, the chloroform is separated from the liquid, and the nitrocinnamic acid is precipitated with sulphuric acid and purified by recrystallisation.

Meyer and Bellmann (J. pr. Ch. **141**, 29) examined the action of bleaching powder on isatoic acid in absence of water by suspending it in chloroform. They obtained an isomeric isatoic acid along with much resinous matter.

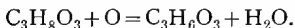
8. Bromine.—This agent is used both in water and in alkaline solution, and frequently substances can be made by its means which cannot be prepared otherwise. Its value for obtaining crystalline oxidation products from sugar was first demonstrated by Hlasiwetz (Ann. **119**, 281). He heated milk sugar (1 mol.) with bromine (4 mol.) and water at 100°, removed the bromine with silver or lead oxide, filtered and precipitated the dissolved metal with hydrogen sulphide, and finally isolated the acid in the form of a crystalline ammonium salt. Later (Ann. **122**, 109), he prepared the acid itself in crystalline form, found that the composition corresponded to the formula $\text{C}_6\text{H}_{10}\text{O}_7$ and named it "isodiglycol-ethylenic acid." Grieshammer (Ar. Pharm. **1879**, 193) obtained an acid isomeric with this by the action of bromine on cane sugar.

Blomstrand (Ann. **123**, 250), in 1862, working about the same time as Hlasiwetz, examined the oxidising action of bromine on substances to which a ring structure is now ascribed. His views as to the action of the bromine in giving rise to certain acids are of historical interest.

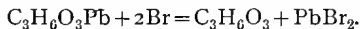
To Fischer, however, belongs the credit of fully recognising the

importance of this oxidising agent in explaining the relations between, and in the synthesis of the members of the carbohydrate group. He also worked out the best methods of employing the agent. Thus in association with Meyer (Ber. **22**, 362) he prepared lactobionic acid by dissolving milk sugar (1 part) in water (7 parts) and adding bromine (1 part) at the ordinary temperature. By shaking frequently, the whole was brought into solution in the course of 24-48 hours. At the end of two more days the solution was warmed slightly, most of the free bromine was expelled by means of a current of air, and the remainder was reduced to hydrobromic acid by means of a current of hydrogen sulphide. The greater part of this was removed by boiling with albumen, and the last traces were precipitated with silver oxide. After finally treating the solution with hydrogen sulphide once more, a filtrate was obtained containing lactobionic acid $C_{12}H_{22}O_{12}$.

Glycerose, the synthetic carbohydrate, he (Ber. **23**, 2,125 ; **20**, 3,385) prepared as follows: Glycerol (10 gr.) and soda (35 gr.) were dissolved in warm water (60 cc.), and bromine (15 gr.) was added when the solution had returned to the temperature of the room. On shaking the mixture the bromine dissolved and carbon-dioxide was evolved. The action was complete at the end of half an hour, and the solution was found to contain a large amount of glycerose, $C_3H_6O_3$, a substance which reduced Fehling's solution—



Its isolation from the solution as glycerosazone, by the action of phenylhydrazine, presented great difficulties. He found, however, that treating lead glycerate with bromine could take the place of the other method of oxidation (Ber. **21**, 2,634), and gave an excellent yield of glycerose—

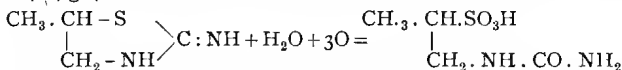


The metal had therefore taken the place of the hydrogen atoms to be removed by oxidation, and the tendency of the metal to unite with the halogen rendered the preparation of the product much easier. He made the lead salt by boiling lead hydroxide, dried at 100° , with 85 per cent. glycerol, precipitating with alcohol and purifying the product.

Kiliani and Kleemann (Ber. **17**, 1,298) added bromine (2 parts) to a cold solution of grape sugar (1 part) in water (5 parts), and agitated the mixture at intervals during 36 hours. By the end

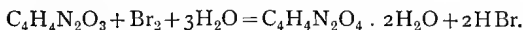
of that time all the bromine had dissolved. They then warmed and shook the liquid over the naked gas flame until the odour of bromine had disappeared. After the solution had cooled, it was restored to its original volume by dilution. The amount of bromine was then determined by analysing a measured portion of the liquid, and by calculation the quantity of lead carbonate was found which would suffice to neutralise the whole of the hydrobromic acid. The carbonate was added a little at a time to the cold liquid, which was subsequently concentrated to half its volume in an evaporating dish over the naked flame. The filtrate was diluted with water, enough silver oxide added to remove any remaining bromine, and the lead and silver in solution were precipitated with hydrogen sulphide. The filtrate, which contained the free gluconic acid, was finally boiled with calcium carbonate, filtered, and evaporated. The concentrated solution deposited gluconate of calcium, $(C_6H_{11}O_7)_2Ca$, the amount formed being 70 grams from 100 grams of grape sugar.

Reformatszky (J. pr. Ch. **149**, 71) prepared the anhydride of a pentatomic alcohol from diallylcarbinol, $C_7H_{11}O(OH)_3$, and found that this substance could not be oxidised any further by the use of bromine. Continuing a research of Gabriel's (Ber. **22**, 1, 142), Rosenthal (Ber. **22**, 2, 987) dissolved propylene- ψ -thiocarbamide (3.5 gr.) in water (200 cc.), neutralised the base with hydrobromic acid, and added bromine water (500 cc.). The precipitate produced by these reagents was redissolved by heating on the water bath, and a clear solution coloured by the excess of bromine was formed. On evaporation this solution left a syrup as residue, which was dissolved in a little water. This solution deposited crystals of β -methyltaurocarbamic acid (2.4 gr.).



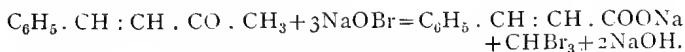
The possibility of obtaining products containing bromine is illustrated by the fate of an attempt of Prager's (Ber. **22**, 2, 993) to oxidise *n*-propylene- ψ -thiocarbamide by this method.

Behrend and Roosen (Ann. **251**, 242) covered isobarbituric acid (4 gr.) with water (30 cc.) and added bromine until a permanent red colour was established, the mixture being well stirred during the process. A quantitative yield of isodialuric acid is obtained partly by spontaneous crystallisation, partly after evaporation over sulphuric acid.



A patented process (Ger. Pat. 21,162), for the preparation of cinnamic acid, shows that the action of bromine in *alkaline solution*

can also give almost quantitative results. Benzylideneacetone (15 parts) is warmed gently on the water bath with a solution of bromine (48 parts) in 4 per cent. caustic soda (650 parts). When the presence of hypobromous acid is no longer perceptible, the interaction is complete (cf. § 7).



Fischer and Hess (Ber. **17**, 563) oxidised methylindole to methylpseudoisatoic acid by means of sodium hypobromite. A halogen derivative of methylindole is first formed, which, on treatment with alcoholic potash, gives the potassium salt of methylpseudoisatoic acid.

9. Chloranil.—This substance, which is now frequently used for oxidising, is best prepared by Gräbe's method (Ann. **263**, 19). Paraphenylenediamine, when treated with potassium chlorate and hydrochloric acid, gives a yellow product which no longer contains nitrogen, and consists of a mixture of tetra- and dichloroquinone in the proportion of 3 : 1. This mixture is used directly as an oxidising agent instead of isolating the pure tetrachloroquinone (chloranil).

It is usually employed in solution in alcohol (Ber. **20**, 515), glacial acetic acid (Ber. **19**, 760), or ether (Ber. **24**, 1,707), or in alcoholic solution acidified with acetic acid. An example of its use is Levi's conversion of the leuco base of thiophene green, tetramethyldiamidodiphenylthienylmethane, into thiophene green by means of an alcoholic solution of chloranil. When the condensation product of benzaldehyde with dimethylaniline, freed from zinc chloride, is warmed with from a half to one part of chloranil at 50–60°, malachite green is formed. Dilute caustic soda is used to remove the chloranil, or chlorinated quinols produced from it, from the mass containing the colouring matter.

The difficulty in finding just the proper oxidising agent for the treatment of leuco bases has been mentioned prominently by von Miller and Plöchl (Ber. **24**, 1,707).

10. Chloric Acid.—This substance is not often used as an oxidising agent, as it too frequently burns up completely the substance submitted to its influence. This was the case in Prager's experiments (Ber. **22**, 2,993) on *n*-phenylpropylene-ψ-thiocarbamide.

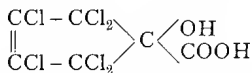
The commercial article always contains barium, as the safe preparation of the acid requires the presence of barium salts.

Feit and Kubierschky (Ch. Z. **1891**, 352) found that bromic acid was still more powerful, but might be used in special cases.

11. Chloride of Iodine.—This substance was used by Poirrier and Chappat (Fr. Pat. 71,970) for the oxidation of methylaniline. The reagent is used diluted with five or six times its weight of water, or a mixture is employed which will produce it in this state (?). The proportions prescribed are : methylaniline (100 parts), iodine (20 parts), and potassium chlorate (20 parts), or methylaniline (1 part), mercuric iodide (3 parts), and potassium chlorate (1 part).

12. Chlorine.—This agent was used by Hlasiwetz and Habermann (Ann. **155**, 123) in preparing gluconic acid from grape sugar. They conducted a current of chlorine through a dilute solution containing 100 grams of grape sugar for several days. After removing the excess of the gas by means of air, the chlorine was precipitated with silver oxide, and, on adding carbonates of barium, cadmium, zinc, or calcium, they obtained the corresponding salt of gluconic acid, $C_6H_{12}O_7$.

Zincke and Küster oxidised hexachloro-cyclopentane oxycarboxylic acid—



by dissolving it in cold water, passing chlorine into the solution, and gradually warming this on the water bath while the addition of chlorine continued. A milky turbidity soon appeared, and after the heating had continued a little longer the vessel was removed from the water bath. When the liquid had cooled, a crystalline mass was deposited, which was recrystallised from petroleum. This was the ketone corresponding to the acid, and the yield was quantitative.

13. Chromic Acid.—This oxidising agent is very widely used, and is employed either in the form of free acid, or of a mixture of a salt with sulphuric acid (cf. §§ 37 and 45).

The solution of chromic acid in water gives a precipitate of chromic oxide, a circumstance which renders its use in this way

inconvenient. Indeed, the formation of the oxide may interfere with the operation where the production of organic acids is in question, since the latter may combine with it to some extent. The chromic acid is therefore almost always used in solution in acetic acid, or else the solution in water is acidified by the addition of sulphuric or hydrochloric acids.

In using glacial acetic acid, Kolbe (J. pr. Ch. **138**, 469) suggests that to regulate the speed of the action it is best to place the chromic acid in a funnel, dissolve it by gradual addition of acetic acid, and let the solution flow into the flask, and thus reach the substance to be oxidised.

Gräbe (Ann. **201**, 356) suggests that the substance be dissolved in acetic acid in a small flask having a constriction in its neck. The chromic acid is placed above a platinum cone, which rests in this constriction, and is gradually dissolved by the condensed acid and washed into the flask.

Seitz (Ber. **23**, 2,257 and 2,259) dissolved chromic acid (27 gr.) in concentrated sulphuric acid (38 gr.) and water (75 cc.), and added the mixture to a solution of α - β -dimethylquinoline (15 gr.) in 20 per cent. sulphuric acid. On heating the mixture on the water bath the chromate, which is at first precipitated, seems to be rapidly attacked by the oxidising agent. After two days' heating the solution becomes green, but still contains a large amount of unchanged substance. After adding excess of ammonia this unchanged material can be driven off with steam. The filtrate from the chromium hydroxide is evaporated to dryness, the ammonia being by this process expelled from combination with the organic acid. The methylquinoline carboxylic acid is extracted from the residue with alcohol.

Meyer (Ber. **23**, 2,259) dissolved orthotoluquinaldine (10 gr.) in dilute sulphuric acid, and added a mixture of chromic acid (30 gr.), concentrated sulphuric acid (40 gr.), and water (100 cc.). The oxidation was complete after the heating on the water bath had been continued for four or five days. He diluted the solution and precipitated the chromium with ammonia, filtered, and then precipitated the sulphuric acid with the calculated amount of barium hydroxide, and filtered again. Finally, the filtrate was evaporated, and the oxidation product extracted from the residue with alcohol.

A very valuable modification of the process, suggested by Hammarsten (Ber. **14**, 71), consists in dissolving the substance in acetic acid in a flask, and running a 10 per cent. solution of chromic acid

in the same solvent into the flask from a burette in portions of 10 cc. at a time. A thermometer is used to note the temperature of the mixture, a convenient height being $45-50^{\circ}$. When further additions of chromic acid produce no rise in temperature, and the green colour of the solution has become tinged with brown, the process is complete. On pouring the liquid into water the new substance is generally precipitated at once.

Dorsch (J. pr. Ch. **141**, 45) dissolved the substance in acetic acid in a flask, and cooled the solution in a freezing mixture until the acid began to freeze on the sides of the vessel. He then added the chromic acid and shook the whole vigorously. The flask was replaced in the freezing mixture, and the temperature was allowed, during twelve hours, gradually to rise to that of the room. Then the warming was continued to 50° , and finally to 80° . After this the oxidation product was precipitated by pouring the solution into cold dilute sulphuric acid.

Rohde (Ber. **22** 267) states that when α - β -dimethylquinoline, dissolved in dilute sulphuric acid, is oxidised with chromic acid sufficient to oxidise one methyl group only, it is easy to separate an acid which is insoluble in water and has the composition of methylquinoline carboxylic acid, $C_9H_5N(CH_3)COOH$.

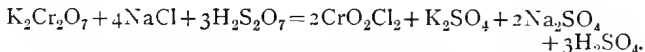
The use of molecular quantities of the substances seems to be generally desirable in oxidations with chromic acid. Thus Holm (Ber. **16**, 1,081) states that when dibromofluorene in acetic acid solution is treated with the calculated amount of the oxidising agent a dibromofluorene ketone, melting at 142.5° , is obtained, while with a slight excess of the agent another modification of the ketone, melting at 197° , is formed.

Then, too, it does not seem always to be a matter of indifference whether acetic acid or dilute sulphuric acid is used as the solvent. Fischer and Van Loo (Ber. **19**, 2,474) found that when β -diquinolyline is boiled in acetic acid solution and the calculated amount of chromic acid is very gradually added, the boiling being continued for 15-20 hours for 5 grams of substance, the solution deposits, on dilution with much water, metaquinoline carboxylic acid. But when they dissolved β -diquinolyline in dilute sulphuric acid, containing equal parts of acid and water, and added a dilute solution of chromic acid drop by drop, an oxidation went on in the cold which could be hastened by finally warming the mixture. When this solution was cooled again it deposited crystals of pyridylquinoline carboxylic acid. As the same agent was used in both cases, the difference in result must have depended on the different solvents employed. In the cases of natural alkaloids, for whose oxidation chromic acid has recently been so popular, this influence of the solvent should probably be taken into account.

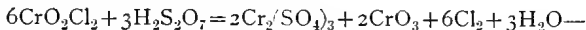
14. Chromyl Chloride.—We owe the first use of chromyl chloride as an oxidising agent for organic bodies to Etard (Ann. Ch. Ph. **1881**, 218). His investigations show that it has the extraordinary property of converting the methyl groups of aromatic hydrocarbons into aldehyde groups, and that the action holds equally for substituted hydrocarbons. Some exceptions to this rule are mentioned below. Thus nitrotoluene is oxidised to nitrobenzaldehyde. By this process the synthesis of aldehydes from hydrocarbons directly is rendered possible. As an intermediate product in this reaction a substance having the formula $x \cdot 2\text{CrO}_2\text{Cl}_2$ is always formed, where x represents an aromatic hydrocarbon. The substance loses 2HCl very easily, giving $x \cdot 2\text{H} \cdot 2\text{CrO}_2\text{Cl}$, and finally water decomposes this, forming the aldehyde.

In many cases the aromatic ring also is itself attacked and a quinone is produced.

Etard *prepared* the *chromyl chloride* by the action of fuming sulphuric acid, salt and potassium bichromate. In making two kilograms of the substance he took a flask of 4–5 litres capacity, and charged it with the materials in the proportions represented by the equation—



Chlorine is given off during the whole interaction. The distillation is stopped when the contents of the flask begin to foam. The yield is 70 per cent. of the theoretical. A secondary reaction expressed by the equation—



accounts for the loss of part of the product and the formation of chlorine.

Moissan (Bull. Ch. **43**, 7) states that when hydrochloric acid gas acts upon chromic acid in a tube it is absorbed, and dark-red fumes of chromyl chloride (b.p. 107°) are given off, and can be condensed in a receiver.

The extremely violent action of undiluted chromyl chloride is illustrated by an unfortunate experiment made by Walter (Ann. Ch. Ph. **66**, 387). On attempting to examine its action upon alcohol he found that the mixture caught fire and exploded, and the experimenter nearly lost his eyesight as a result of the accident. A little later Carstanjen (J. pr. Ch. **110**, 51) attempted to use it

with acetic acid as diluent, but with no better success. The proper choice of a diluent seemed to be of the utmost importance, and Etard found that carbon disulphide was the most suitable one for most purposes. For example, a 10 per cent. solution of chromyl chloride in carbon disulphide is poured into an equally dilute solution of toluene in the same solvent. If necessary, external cooling is applied to prevent the solution boiling. It is preferable to keep adding the former solution as long as it is decolourised, as this gives a better result than using the theoretical quantity. When the precipitate, which is formed during the addition, is decomposed with water, benzaldehyde is formed. Etard states that nitrobenzene is oxidised to nitroquinone by this process. But Henderson and Campbell were unable to repeat the experiment, and suggested that Etard's substance must have contained nitrotoluene and that his product was *p*-nitrobenzoic acid.

As a further illustration of the use of chromyl chloride, Bornemann's (Ber. **17**, 1,464) very exact description of the method of preparing *m*-toluylaldehyde may be given. It shows incidentally that Etard's process does not exclude all possibility of explosion.

He took a little more than one molecular proportion of metaxylene (35 parts) and two molecular proportions of chromyl chloride (100 parts), and diluted them with carbon disulphide in the proportion 15 : 100. He then added the latter solution, 10-15 grams at a time, to the former. After a time, a brown crystalline precipitate began to collect on the bottom of the vessel. At the same time the temperature rose and cooling had to be resorted to. If care was not taken to wait, after each addition, until the red colour had given place to a chocolate-brown shade, and the rise of temperature had subsided, disagreeable explosions occurred. The whole operation lasted about seven hours. At the end of twelve hours more, the precipitate had completely subsided, and the supernatant liquid was colourless. The precipitate was collected in a funnel plugged with glass wool, and washed with carbon disulphide. The substance was then placed in a closed dry flask on the water bath, and the carbon disulphide vapour was removed by connecting the interior with a pump. After this treatment had lasted forty-five minutes, a perfectly dry, very hygroscopic substance remained behind. It was not advisable to continue the heating beyond this point, as a violent emission of gas was apt to occur which burst the flask. The solid was then thrown into cold water in small quantities at a time, when it decomposed into *m*-toluylaldehyde, chromic acid, and

chromic chloride. As the chromic acid oxidised the aldehyde, if they remained in contact, it had to be removed by leading sulphur dioxide into the mixture, and then immediately driving the aldehyde over with steam. Or the aldehyde could be secured by rapidly extracting the mixture with ether. For further purification the aldehyde was converted into its compound with sodium bisulphite.

To effect this, the ethereal solution was violently shaken with a concentrated solution of sodium bisulphite. Bornemann found that unless all these precautions were observed satisfactory results could not be obtained.

Richter (Ber. **19**, 1,061) prepared *p*-nitrobenzaldehyde by the same process. He was unsuccessful however in an attempt to prepare dinitrobenzaldehyde from dinitrotoluene. Etard himself states that for the oxidation of acids like benzoic acid and acetic acid this agent is not serviceable.

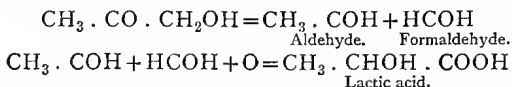
Using the process of Etard, v. Miller and Rohde (Ber. **23**, 1,074) found that propylbenzene gave benzylmethylketone in place of its isomer hydrocinnamic aldehyde, not a trace of the latter being formed. From isopropylbenzene (Ber. **24**, 1,358) they obtained hydratropic aldehyde and acetophenone, which they separated by means of sodium bisulphite.

15. Copper Solution—Alkaline.—This agent is used as an oxidiser chiefly for grape sugar, but it has also been used for synthetic purposes with many other substances.¹ Thus Böslér (Ber. **14**, 327) found in it the best oxidising agent for the conversion of anisoin into anisil. Anisoin (1 part) is dissolved in hot 70 per cent. alcohol (5 parts), and the alkaline copper solution is added until a permanent blue tint remains. The solution is then filtered from cuprous oxide, and the anisil precipitated with water. The yield is quantitative.

Breuer and Zincke (Ber. **13**, 639) dissolved acetyl carbinol (1 mol.) in 20 parts of water, and added caustic soda (6 mol.) A

¹ Alkaline copper solutions play an important part in the chemistry of the carbohydrates because cane sugar, starch, etc., can all be converted into grape sugar by boiling with dilute acids (Kirchoff, 1811). In 1819, Braconot showed that cellulose was inverted by the same treatment. Fehling's solution, in which tartaric acid is used to retain the cupric oxide in solution, has the disadvantage of not keeping well. When mannite is used (Schmiedeberg, A. Path. Pharm. **28**, 363) a solution is obtained which serves equally well for the quantitative determination of sugar, and can be kept unchanged for years.

solution of cupric sulphate (2 mol.) was then allowed to run in, and the whole was warmed on the water bath. The following equations represent the actions :—



After trying other oxidising agents, E. Fischer (Ann. **211**, 229) found in the alkaline copper solution a suitable agent for converting benzfuroin into benzfural. He dissolved benzfuroin (2 parts) in warm alcohol (35 parts), and added a weak alkaline copper solution (70 parts) and enough water to cause the two liquids to mix. The temperature was kept at 50°, and the oxidation was quickly completed. As soon as a filtered sample of the liquid ceased to reduce Fehling's solution in the heat, the whole was diluted, filtered, and extracted with ether. The oxidising agent was prepared by dissolving crystallised cupric sulphate (6 parts) with the requisite amounts of tartaric acid and caustic soda.

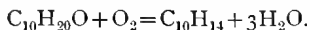
16. Cupric Acetate.—Baeyer (Ber. **24**, 2,693) oxidised a very unstable hydrazo-compound in absence of water by dissolving one gram of it in 15 cc. of warm absolute alcohol, and adding to the boiling liquid a hot saturated solution of 0·7 grams of neutral cupric acetate containing a drop or two of acetic acid. When the liquid, which became red from separation of cuprous oxide, was filtered into ice, yellow needles of the oxidation product soon separated.

17. Cupric Oxide and Hydroxide.—When leucaniline hydrochloride is mixed with cupric oxide and heated to 120-160°, it is converted into fuchsine (Ger. Pat. 19,484). This seems to be the only application of this agent to the synthesis of organic bodies.

For the oxidation of various carbohydrates, Habermann and König (M. f. Ch. **5**, 208) frequently boiled them for several hours in alkaline or neutral solution with cupric hydroxide. Treated in this way, galactose gave carbon dioxide, formic acid, glycollic acid, lactic acid, and other undetermined acids.

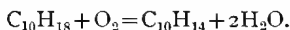
18. Cupric Sulphate.—By dry oxidation with anhydrous cupric sulphate, Brühl (Ber. **24**, 3,374) converted menthol easily into cymene. When the substances had been heated for several hours at 250-280° and the tube was opened, streams of sulphur

dioxide issued, and cupric oxide saturated with an oil remained behind. If a small amount only of cupric sulphate is used, the reduction may be carried so far as to give hydrogen sulphide and cupric sulphide. The oil was found to be nearly all volatile with steam, and turned out to be cymene—



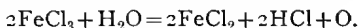
When chromic acid was tried as an oxidising agent, menthone was formed, while permanganate gave oxymenthyllic acid with pimelic and other fatty acids.

He obtained the same substance (Ber. **25**, 143) by heating menthene with cupric sulphate at 250° .



The following example will illustrate the use of cupric sulphate on a large scale (Friedländer, *Farbenfabrikation*, 33). Pure dimethylaniline is mixed with a large amount of dry salt or chalk (Ger. Pat. 32,829), for the purpose of keeping it in a state of fine division. It is then heated for 8–10 hours at $50\text{--}60^\circ$, with 50 per cent. of pulverised cupric sulphate and 20 per cent. of liquid phenol (containing cresol). The phenol probably acts as an oxygen carrier by being converted into quinone derivatives. Methyl violet is prepared from the product.

19. Ferric Chloride.—This substance is usually applied in solution in water, and, if necessary, at the boiling temperature. The action takes place according to the equation—

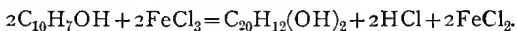


It will be noticed that hydrochloric acid is set free by the action. The following admirable method was used by Baeyer (Ber. **15**, 775) to avoid the inconvenience arising from this cause. He found that ethyl indoxanthinate was best prepared by the oxidation of ethyl indoxylate by means of ferric chloride. Yet the operation was one of the most delicate in the whole investigation of the indigo group, for the hydrochloric acid decomposed the ethyl indoxanthinate, and in addition to this there was danger of the action stopping halfway at an intermediate product. The ethyl indoxylate (1 part) was dissolved in acetone (4 parts), and ferric hydroxide freshly precipitated from crystallised ferric chloride (2 parts) was added. In another vessel, crystallised ferric chloride (4 parts) was dissolved in acetone (4 parts). Both solutions were warmed to 60° and mixed,

and a dark-green solution was obtained. This was diluted with a large amount of water, also at 60°, and the mixture, which became yellow, was filtered from the ferric hydroxide and extracted with ether.

Fischer and Busch (Ber. **24**, 1,871) prepared the corresponding azonium base from a hydroquinoxaline very easily by dissolving the latter in boiling alcohol and adding aqueous ferric chloride.

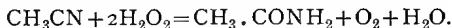
Solutions of ferric chloride in glacial acetic acid have also been used. Dianin found this an excellent method for oxidising naphthols to dinaphthols. With a similar object in view, Witt (Ber. **21**, 728) dissolved *p*-tolyl-naphthylamine (10 gr.) and solid ferric chloride (10 gr.) each in acetic acid (40 cc.), mixed the solutions, and boiled for some time. He obtained the corresponding substance of the dinaphthyl series. The yield was only 4 grams, but chromic acid did not give even a trace of the dinaphthyl base either in hot or cold solution—



20. Ferric Hydroxide.—This substance is recommended for the oxidation of leuco bases (Ger. Pat. 19,484). Thus, when an intimate mixture of leucaniline with excess of ferric hydroxide is heated at 120–160° in open or closed vessels, a metallic-looking, green-coloured fused mass is produced. This is boiled with water to extract the dye, which is precipitated by adding salt.

21. Hydrogen Peroxide.—This is a very valuable agent, and many oxidations can be conducted quantitatively by its means.

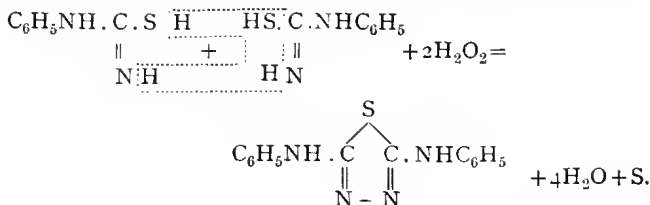
Radziszewski (Ber. **18**, 355) has shown that it converts nitriles into amides with evolution of oxygen—



The reaction goes with special ease in alkaline solution and at 40°. Thus, when benzonitrile and caustic potash are added to peroxide of hydrogen, and the mixture is shaken, a quantitative yield of benzamide is obtained. Even cyanogen is converted, by 3 per cent. hydrogen peroxide and a drop of caustic potash, quantitatively into oxamide.

Hektor (Ber. **22**, 1,177) oxidised phenylthiourea by its means as follows: The substance (5 gr.) was dissolved in fifty per cent. alcohol with a few drops of hydrochloric acid, and three per cent. hydrogen peroxide (40–50 gr.) was added in small portions at a

time. The liquid became turbid from separation of sulphur. This was removed by filtration, and the warm liquid, when neutralised with alkali, gave a quantitative precipitate of dianilidoazothiols—



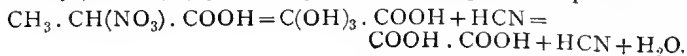
Bernthsen (Ber. **20**, 937) succeeded in oxidising juglone to oxyphthalic acid by means of alkaline hydrogen peroxide, although the action did not go as smoothly as either of the above examples.

The action of hydrogen peroxide is frequently used in attempts to determine the constitution of alkaloids. Wolffenstein (Ber. **25**, 2,777) and Merling (Ber. **25**, 3,124) have used it in this way. The latter transformed bases of the pyridine series into oxy-bases. Thus when α -methyltropidine (1 part) is frequently shaken with ordinary hydrogen peroxide (15 parts) for several days at the temperature of the room the conversion into the oxy-base is quickly completed.

The observation of Leeds (Ber. **14**, 977) that benzene is partially converted into phenol by boiling for sixty hours with 1·2 per cent. hydrogen peroxide is of considerable theoretical interest. The direct conversion of benzene into phenol was first attained by Schultzen and Naunyn (P. Ar. **12**, 294) by feeding dogs with benzene.

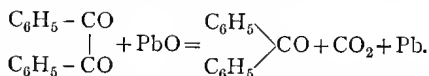
22. Hydroxylamine.—The oxidising influence of this substance has frequently been noticed. Thus Meyer (J. pr. Ch. **137**, 497) states that when oxanthranol is heated with the hydrochloride and a few drops of hydrochloric acid for 2–3 hours at 160–170°, ammonium chloride and anthraquinone are formed, and a part of the latter is converted into an oxime. Similarly croconic acid (Ber. **19**, 305) is converted by it into the pentoxime of leuconic acid. Even under these conditions, however, its action frequently takes a quite different direction (Ber. **20**, 614), so that the substance can hardly be regarded as an oxidising agent.

23. Internal Oxidation.—An example of this is the oxidation of nitrolactic acid to oxalic acid and hydrocyanic acid, observed by Henry (Ber. **12**, 1,837). He gives the rather peculiar equations :

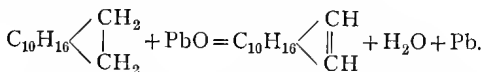


He explains by this reaction the occurrence of hydrocyanic acid, which is characteristic of all oxidations with nitric acid. In Gmelin-Kraut's "Handbuch der organischen Chemie" (4th ed., p. 303), a number of statements have been collected showing that this fact has been known since the beginning of the century.

24. Lead Monoxide.—This oxidising agent is used either by mixing it with the substance and distilling from a retort, or by conducting the vapour over the heated oxide. Thus Wittenberg and Meyer (Ber. **16**, 502) led the vapour of benzil over lead oxide and obtained benzophenone—



By the same process Behr and van Dorp (Ber. **6**, 753) prepared acenaphthylene from acenaphthene—



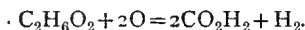
25. Lead Peroxide.—The oxidising power of this substance is generally utilised by adding it to a solution of the material to be oxidised either in the cold or in the heat.

According to Fehrmann (Ber. **15**, 1,882), the oxide is best obtained by mixing a warm (60°) concentrated solution of lead chloride with a solution of bleaching powder. The latter is added until a filtered sample gives no further brown colour on addition of a drop of the same reagent. The precipitate is filtered and washed, access of air being avoided during the process. When dry it forms an almost black powder, but it keeps better in the moist condition.

It is one of the most valuable agents for oxidising leuco bodies. For example (Ger. Pat. 50,782), a leucosulphonic acid (100 parts) is dissolved in water (400 parts) and 35 per cent. caustic soda (31 parts). In another vessel lead peroxide, containing 34 per cent. of PbO_2 (120 parts), is stirred up with water (1,500 parts). The first solution is cooled to 20° and added to the second, and then immediately afterwards a cold (20°) solution of sulphuric acid of sp. gr. 1.842 (45 parts) in water (300 parts) is mixed with the other two. The whole is stirred for a short time and then neutralised by the addition of a solution of soda (30 parts) in water (200 parts).

The lead precipitate is filtered off and the dye thrown down by addition of common salt in the solid form.

Gläser and Morawsky (M. f. Ch. **10**, 578) noted the extraordinary fact that, when lead peroxide acts upon dilute alkaline solutions of alcohol, glycol, cane sugar, and other similar substances, hydrogen gas and formic acid are produced. In the case of glycol the equation is :



26. Manganese Dioxide.—This substance is sometimes used in the form of pyrolusite, but more frequently as precipitated hydrated or anhydrous manganese dioxide.

E. and O. Fischer (Ber. **12**, 796) oxidised the leuco base of malachite-green by treating a cold solution of the base in dilute sulphuric acid with finely divided pyrolusite.

Schmidt and Wilhelm (Ar. Pharm. **1888**, 347) added gradually finely pulverised pyrolusite (7·5 gr.) to a boiling solution of hydrastine (5 gr.) in water (75 gr.) and sulphuric acid (5 cc.). They boiled the mixture as long as any gas was evolved, and then filtered. When it cooled the whole mass became filled with crystals of opianic acid, and hydrastinine was found in the mother-liquor.

Donath (Ch. Z. **1888**, 1,191) found that when the vapour of alcohol was conducted over pyrolusite heated to 150–360° it was mostly converted into acetone.

Carius (Ann. **148**, 51) obtained some rather extraordinary results by using this oxidising agent. He mixed a cold solution of pure sulphuric acid (600 gr.) in water (120 gr.) with benzene (100 gr.) and finely pulverised pyrolusite (100 gr.), and shook them till an emulsion was formed. The flask was immersed in water from time to time to keep the temperature below 20°. After the mixture had remained for several days it was examined and found to contain formic acid, benzoic acid, and phthalic acid. A satisfactory explanation of their formation has not yet been given.

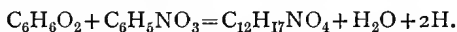
Döbereiner (Ann. **3**, 144) first made the observation that on boiling a solution of tartaric acid with pyrolusite and sulphuric acid carbon dioxide and formic acid are produced. Liebig prepared formic acid by treating starch (100 gr.) with pyrolusite (370 gr.), sulphuric acid (300 gr.), and water (300 cc.). He obtained 33·5 grams.

Formic acid is now much more readily prepared by Berthelot's process from oxalic acid (Ann. **98**, 139). It seems, however, that formic ether is still manufactured by the following process (Dingl.

Polyt. Jour. **187**, 402): Starch (4·5 kg.), and pyrolusite, containing at least 85 per cent. of MnO_2 (14·5 kg.), are placed in a vessel, and upon them is poured a cold mixture of sulphuric acid (14 kg.), water (2·5 kg.) and 80 per cent. alcohol (7·5 kg.). After the action has been started, further external heating is unnecessary. At first alcohol comes over, then commercial formic ether. The free acid in the latter is neutralised with calcium hydroxide. When, finally, heat is applied, a liquid containing much formic acid passes over.

Precipitated manganese dioxide, or its hydrate, is chiefly employed for oxidation in acid solutions such as those of bases in sulphuric acid or acetic acid. Pyrolusite or hausmannite is frequently added as well.

Nietzki (Ber. **24**, 3,367): dissolved molecular proportions of nitroresorcinol (10 parts) and resorcinol (15 parts) in cold alcohol, and suspended manganese dioxide (1 mol.) in the solution. He then cooled the mixture and added sulphuric acid (2 mol.) diluted with an equal volume of water. After a short time the liquid became cherry-red. By precipitating the filtered solution with water resazurin was thrown down—



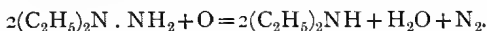
27. Mercuric Acetate.—Tafel (Ber. **25**, 1,619) states that this is a suitable oxidising agent for converting derivatives of piperidine and tetrahydroquinoline into the corresponding derivatives of pyridine and quinoline. Thus quinoline itself is easily made from tetrahydroquinoline by heating with a solution of mercuric acetate at 150° . Metallic mercury is formed at the same time (cf. § 48).

28. Mercuric Chloride.—This substance is specially recommended by Goldberg (Ber. **24**, 3,553) for the preparation of fuchsine. He heats a mixture of paratoluidine (1 mol.) and aniline (2 mol.) with the theoretical amount of mercuric chloride for an hour and a half at 180 – 200° . Fuchsine prepared in this way is mixed with almost none of the coal-like amorphous substances which are always formed when arsenic acid or other oxidising agents are used.

29. Mercuric Nitrate.—Gerber and Keller (Jahresb. **1860**, 720) used mercuric nitrate as an oxidising agent in the preparation of fuchsine.

30. Mercuric Oxide.—Both the red and the yellow varieties of mercuric oxide are frequently used as oxidising agents.

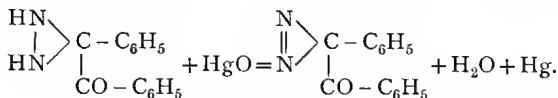
E. Fischer (Ber. **11**, 2,209) added yellow mercuric oxide gradually to a cold solution of diethylhydrazine in water until the oxide was no longer reduced. The solution became turbid from separation of an oil which was taken up mechanically by the mercury compounds. These were separated by filtration and the oil was extracted from them with alcohol. It was found to be tetraethyltetrazone, $(C_2H_5)_2N.N:N.N.(C_2H_5)_2$. The action is therefore quite different from that of Fehling's solution, which converts diethylhydrazine almost entirely into diethylamine and nitrogen—



Heffter (Ber. **22**, 1,049) boiled a 10 per cent. solution of glucose with yellow mercuric oxide until no further reduction took place. The warm solution was filtered from the mercury and mercurous oxide, and on cooling gave an excellent yield of the crystalline mercurous salt of gluconic acid.

Börnstein and Herzfeld (Ber. **18**, 3,354) found that a solution of levulose in water could be boiled with red mercuric oxide without being attacked, but that the addition of a drop of barium hydroxide brought about instant oxidation. The red colour of the oxide changes at once into the black of mercurous oxide. In carrying out the process it is advisable to add alternately mercuric oxide and barium hydroxide. The levulose is largely converted into trioxobutyric acid and glycolic acid. Herzfeld (Ann. **245**, 27) tried this method with glucose and obtained chiefly gluconic acid.

Curtius (Ber. **22**, 2,162) obtained the calculated amount of monoketazobenzil by shaking a solution of monohydrazobenzil in benzene with mercuric oxide—



Fischer and Hepp (Ann. **256**, 252) obtained complicated oxidation products by boiling tetranilidonaphthalene in benzene solution with mercuric oxide.

31. Nitrobenzene.—The oxidising power of this substance is chiefly known from its use by Coupier in the preparation of fuchsine. The method consists in heating a mixture of aniline, toluidine, nitrobenzene, and nitrotoluene with some hydrochloric acid and a little zinc chloride at 180–190°. The yield of fuchsine, about 38 per cent., is not very different from that obtained by the older method, by use

of arsenic acid, but the present method has the advantage of avoiding the use of this very poisonous substance.

It has seldom been used for oxidation in the laboratory. Lellmann and Geller (Ber. **21**, 1,921) heated piperidine (5 gr.) with nitrobenzene (22 gr.) for four hours in a sealed tube at 250–260°. They obtained some pyridine, but the yield was unsatisfactory.

32. Nitric Acid.—Oxidation with nitric acid is generally carried out in the traditional manner by boiling the substance, often for several days, with the more or less diluted acid, a large excess of the latter being always taken. As Krafft remarks (Ber. **21**, 2,735), this leads frequently to the formation of secondary products by the continued action of the acid. Indeed the amount of these is often greater than that of the substance sought. Krafft found that it was frequently better to pour the substance to be oxidised into a quantity of cold nitric acid whose temperature is kept between 0° and 10°. With one part of the substance, from one to three parts of the acid of sp. gr. 1.5 are taken. When the first phase of the action seems to be complete, the mixture is slowly heated to 50°. The course of the action can often be followed by observing the appearance of the mass. Thus the effervescence may cease or coloured intermediate products may disappear. In all cases caution must be used, but when successful this method occupies at most only a few hours, and the quantity of secondary products is reduced to a minimum. Of course this process is entirely inapplicable to aromatic substances, as they are converted into nitro-derivatives by such treatment.

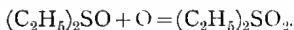
This method will naturally be used where a convenient reaction showing the presence of the unchanged substance is available.

For example, Schmiedeberg and Meyer (Z. physiolog. Ch. **3**, 444) oxidised camphoglycuronic acid by warming it in a flask connected with a condenser with dilute nitric acid. As the original substance reduces Fehling's solution, they were able, by testing with this reagent, to ascertain when it was all decomposed. They then neutralised most of the nitric acid and distilled the product, adding water from time to time, in order to separate any volatile acids which might have been formed. They neutralised the distillate with lime, extracted a little campherol which had passed over with ether, and reduced the nitric acid to ammonia by adding caustic potash and zinc dust. Finally, they obtained formic acid by filtering the liquid, acidifying with sulphuric acid, and again

distilling. They identified it by means of the lead salt. It is a difficult matter to demonstrate the formation of formic acid in oxidations with nitric acid, because, as Ballos (Ber. **17**, 9) has shown, it is converted by this agent in the heat into carbon dioxide, water, and even to a large extent oxalic acid.

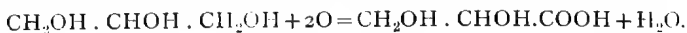
Siegfried (Ber. **24**, 421) used lead hydroxide for eliminating the nitric acid after the oxidation was completed. The hydroxide when precipitated in the cold and carefully washed is best preserved under water. It dissolves in the latter to some extent in the colloid form. A large excess of it, when added to an acid mixture, precipitates the acid as basic nitrate. So that even without boiling the solution which is basic from the presence of the dissolved hydroxide, a proceeding which might lead to decomposition, the acid can be completely eliminated. The dissolved lead is removed from the filtrate with hydrogen sulphide.

Substances which are hard to oxidise may be treated with nitric acid in sealed tubes. Thus sulphoxides are easily converted into sulphones by heating with fuming nitric acid for a considerable time at 100°—



When it is desired to use nitric acid for the oxidation of aromatic bodies with fatty side chains, it is best to boil with dilute nitric acid to avoid the formation of nitro-derivatives. In many such cases, however, a nitrate can be substituted for the nitric acid, and all danger of the formation of nitro-derivatives avoided. The preparation of benzaldehyde (Lauth and Grimaux, Ann. Ch. Pharm. **143**, 186) from benzyl chloride and an aqueous solution of lead or copper nitrate is an example of this.

Debus (Ann. **106**, 80) suggested the method of placing a layer of nitric acid above or below the substance in order to moderate the action of the nitric acid. Thus he diluted glycerol (1 part) with a little more than an equal bulk of water, placed it in a cylinder, and passed down to the bottom, through a long funnel, nitric acid of sp. gr. 1.5 (1 part). The two layers gradually mixed and became blue in colour. He stated that five or six days were required to complete the action, but found later that exposure to sunlight not only improved the yield, but also reduced the time to twelve hours. The product is glyceric acid—



When the substances are mixed together, oxalic acid is the chief product, and very little glyceric acid is found. The brilliant work of Fischer and Tafel (Ber. **20**, 1,089), which has led to the synthesis of sugar, has shown that aldehydes or ketones are formed as intermediate products. These had remained unnoticed, not to say unisolated, for want of suitable methods. On addition of phenylhydrazine they are precipitated as osazones.

Very remarkable are the results obtained by V. Meyer and Wachter (Ber. **25**, 2,632), by dissolving orthiodobenzoic acid in fuming nitric acid, boiling for a few minutes to complete the action, and finally pouring the solution, when cold, into water. An acid is thrown down which they name iodosobenzoic acid, $C_6H_4 \begin{matrix} \diagup I=O \\ \diagdown COOH \end{matrix}$. Iodobenzene and iodoxybenzene, $C_6H_5IO_2$ have since been obtained by Willgerodt (Ber. **26**, 358).

The substances formed by the action of nitric acid frequently either separate spontaneously or are thrown down on addition of water. Sometimes they are extracted by some suitable solvent from the diluted solution. As the products of the action of nitric acids are usually acids, it is often sought to precipitate them in the form of insoluble salts, and so separate them from the nitric acid whose salts are all soluble. When no insoluble salt can be found, a separation by crystallisation may be attempted.

Apart from ways already mentioned of getting rid of the nitric acid, it can often be removed by evaporation, water being added from time to time to prevent the acid which remains becoming too concentrated (cf. Chap. XVII. § 14).

33. Nitrous Acid.—Nitrous acid, which is best prepared by heating arsenious oxide with 50 per cent. nitric acid (cf. Chap. XIII. § 2), is a much more convenient oxidising agent than is usually supposed. This unpopularity may have arisen from the fact, ascertained by Lenssen (J. pr. Ch. **82**, 307) in comparing various oxidising agents in regard to their applicability to titration, that it is not in our power to determine its reduction to the stage of NO, N_2O , or N_2 at will. This seems to depend on conditions such as the temperature and the duration of the action.

It is a very mild oxidising agent. For example, Benedikt and Hübel (M. f. Ch. **2**, 323) found that dinitrosoresorcinol was at once converted into trinitrosoresorcinol by dilute nitric acid, while potassium permanganate and potassium ferricyanide decomposed it com-

pletely. But when it was suspended in ten parts of ether, and nitrous acid was led into the mixture until the substance dissolved, and the nitric acid which was formed was removed by washing with water, the desired product, dinitroresorcinol, was easily obtained.

Hydrocollidine dicarboxylic ether is entirely decomposed by nitric acid, while potassium permanganate gives at once lutidine tricarboxylic acid. Collidine dicarboxylic acid can only be obtained by the use of nitrous acid. Hantzsch (Ann. **215**, 21) mixed the ether with an equal amount of alcohol, cooled the mixture, and led nitrous acid into it until a sample of the liquid formed a clear solution in dilute hydrochloric acid. Much heat is given out, and the portion of the substance not at first dissolved, goes later into solution in the alcohol. When the alcohol is evaporated and sodium carbonate in excess is added, the collidine dicarboxylic ether is thrown down as an oil which, after being dried, shows a constant boiling-point. The yield is quantitative.

According to Wallach (Ber. **5**, 256), a large amount of nitrous acid dissolves in chloral and the liquid becomes green. When this stage has been reached it is sealed up in a tube, and heated for an hour in the water bath. On account of the great pressure produced only a little of the substance can be enclosed in each tube. When the tube is opened the contents solidify to a mass of trichloroacetic acid, if the amount of nitrous acid has been sufficient. The acid is purified by pressure between sheets of filter paper. It is possible that other aldehydes, free from halogen, may be equally easily oxidisable by this reagent, and that it may therefore take the place of the silver oxide or oxygen which has hitherto been in use.

34. Oxygen.—Oxygen may be prepared in Kipp's apparatus as follows (Baumann, Z. ang. Ch. **1890**, 79): The middle bulb of the apparatus is filled with pure pyrolusite in pieces of the size of a pea. To prevent the substance falling into the lower bulb, a rubber ring covered with long-fibred asbestos is placed over the annular opening connecting the two. The fluid is prepared by pouring gradually 150 cc. of sulphuric acid into a litre of ordinary peroxide of hydrogen, which is cooled during the process. According to Blau (M. f. Ch. **13**, 280) oxygen entirely free from nitrogen may be obtained by the action of hydrogen peroxide on potassium bichromate.

Oxygen is usually applied in oxidation by conducting the gas through the liquid to be treated. For example, Müller (Ber. **22**,

857) dissolved triamidobenzene hydrochloride (10 gr.) and sodium acetate (18 gr.) in water (200 cc.), warmed the solution, and led oxygen through it for two or three hours. Probably triamidophenazine was formed in accordance with the equation—



Michaelis and Lampe (Ber. **24**, 3,739) state that when phenylpyrazolidine is placed on a watch glass it loses two atoms of hydrogen and forms phenylpyrazoline.

The activity of oxygen is much increased by adding *platinum black* to the liquid. Thus Grimaux (Bull. Ch. **45**, 481) obtained by this process from glycerol a liquid which reduced Fehling's solution, so that, in view of Fischer and Tafel's work, he must have had a solution of glyceric aldehyde. Oxidations similar to this were made by Demole and Dürr (Ber. **11**, 315 and 1,302).

Loew (Ber. **23**, 289) states that the catalytically most powerful platinum black is prepared as follows: Platinum tetrachloride (50 gr.) is dissolved in water (50–60 cc.) and a 40–45 per cent. solution of formaldehyde (70 cc.) is added. This mixture is thoroughly cooled, while caustic soda (50 gr.) dissolved in an equal weight of water is added. The greater part of the metal is at once precipitated. The mixture is filtered at the end of twelve hours, and a yellow liquid passes through the filter, which deposits a little more platinum on being boiled. When the greater part of the sodium chloride and formate has been washed out, a black liquid runs through produced by the solution of a part of the very fine powder. The washing is therefore interrupted at this stage until a process of oxidation which begins on the filter is completed. The moist black substance begins to absorb oxygen from the air, and for several hours a rustle, caused by the breaking of small gas bubbles all over the precipitate, may be heard. The black substance turns into a porous mass during this process, and is finally washed free from sodium chloride, whose presence greatly interferes with the activity of the platinum, as Döbereiner had already shown. The powder is finally dried over sulphuric acid.

Platinised asbestos, which is also useful for oxidation, was prepared by Weidel (M. f. Ch. **8**, 121) by intimately mixing asbestos (100 gr.) with platinum black (80 gr.). Tischtschenko (Ber. **20**, 704c) states, however, that it should not contain so much platinum, and should not be black but gray. Lunge (Sodaindustrie, **1**, 601) says that the platinised asbestos used in the preparation of sulphur

trioxide from sulphur dioxide and oxygen in manufactories contains only eight per cent. of platinum. Platinised quartz, recommended by Zulkowski and Lepéz (M. f. Ch. **5**, 538), may be better than platinised asbestos.

Oxygen carriers, similar to the chlorine carriers, are known. The most active substance of this nature has been shown by Loew (J. pr. Ch. **126**, 300) to be a solution of cupric oxide in ammonia. Nitrogen compounds particularly, when mixed with this substance and shaken with air, seem to undergo profound changes.

He neutralised uric acid (1 gr.) with the theoretical amount of caustic potash, placed it in a flask with the copper solution (100 cc.), and allowed it to remain in a warm place for several days. During this time it was frequently shaken, and the air was periodically renewed. The liquid was then evaporated and nearly neutralised with sulphuric acid. An acid reaction must be carefully avoided on account of the nitrite which is formed. The mass was dried on the water bath and extracted with alcohol. Urea and a large amount of oxalic acid went into solution. Amidoacetic acid and amidosuccinic acid are similarly attacked under such circumstances, producing oxalic acid and carbon dioxide.

L. Meyer (Ber. **20**, 3,058) investigated a number of salts in regard to their power as oxygen carriers, and found that manganous sulphate was the most active of those examined.

35. Ozone.—The action of ozone upon organic bodies has been known for years (Ann. **125**, 207). Great care has to be exercised in its use, as substances of quite extraordinary explosive power are frequently formed. Houzeau and Renard (C. R. **76**, 572) obtained such a body by its action on benzene, and named it ozobenzene. Nencki and Giacosa (Z. physiolog. Ch. **4**, 340) were able to prepare very small quantities of phenol from benzene in the same way. Berthelot (C. R. **92**, 895) speaks of an excessively explosive liquid which he obtained by its action on absolute ether.

In opposition to these statements, Leeds (Ber. **14**, 975) asserts that, when ozone acts upon benzene, carbon dioxide, oxalic acid, formic acid, and acetic acid along with a black amorphous substance are formed. He found no ozobenzene. He also studied the action of nascent oxygen prepared by covering phosphorus with water and exposing it to the air. In absence of benzene, ozone was produced. But when benzene was added the ozone reaction could not be obtained. Under these circumstances, when the mixture was

exposed to sunlight phenol and oxalic acid were formed. In diffused light oxalic acid was formed but not phenol. The most active form of oxygen has already been mentioned (cf. Chap. XV, § 8).

36. Platinum Tetrachloride.—This salt is seldom used for oxidation on account of its expensiveness. Platinum black and platinised asbestos, as we have already seen (cf. § 34), assist very energetically the action of free oxygen and air.¹

Schmidt and Wilhelm (Ar. Pharm. **1888**, 350) dissolved hydrastine five grams at a time in dilute hydrochloric acid, added excess of platinum tetrachloride, and boiled the solution for six hours in a flask connected with an inverted condenser. The liquid gradually acquired a dark-red colour. On being filtered from the deposited platinum and cooled, white needles of opianic acid and crystals of a platinum double salt, which could be easily separated with ether, appeared. A further batch of crystals was obtained on evaporation. The double salt was hydrastinine-platinous chloride, $(C_{11}H_{11}NO_2 HCl)_2PtCl_2$.

Dullo (J. pr. Ch. **78**, 370) states that platinum dissolves very rapidly in aqua regia without leaving any residue when the operation is conducted under pressure. A flask is used which is connected with a bent glass tube, whose longer limb dips about a metre beneath the surface of a cylinder of water. The vapours from the acid can easily overcome this pressure, and the solution of the metal occupies very little time.

37. Potassium Bichromate.—Until this salt was largely replaced by sodium bichromate, the reagent known as chromic acid mixture, in which the chromic acid was set free from potassium bichromate by means of dilute sulphuric acid, was one of the most generally used oxidising agents. Usually forty parts of bichromate and fifty-five of sulphuric acid, the latter diluted with twice its volume of water, are taken. This mixture is added to that containing the substance to be oxidised either at once or in a fine stream. The reaction is frequently incomplete in the cold and has to be assisted by boiling the mass. The first careful investigation of the

¹ These substances seem also to have the power of increasing the activity of other elements. For example, Debus states (Ann. **128**, 200) that methylamine is formed when hydrocyanic acid and hydrogen are led over platinum black.

applicability of bichromate in solution for the purpose of oxidation was made by Penny (J. pr. Ch. **55**, 210), who sought a liquid which could be used in titrating.

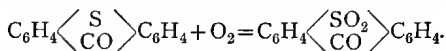
Pfeiffer (Ber. **5**, 699) oxidised isobutyl alcohol (100 gr.) by mixing it with water (750 cc.) and a solution of chromic acid (95 gr.) in a retort. Lipp (Ann. **205**, 2) used the corresponding amount of potassium bichromate dissolved in five times its weight of water in place of the latter, and added the amount of sulphuric acid necessary to set the chromic acid free. He warmed the alcohol and water to 70–80°, and allowed the oxidising mixture to drop into it from a funnel provided with a stop-cock. The author found that it was advantageous to lead carbon dioxide through the solution during the process, so as to facilitate the distillation of the aldehyde and prevent its being oxidised further. The aldehyde was extracted from the distillate by shaking with sodium bisulphite and was finally isolated by redistilling the bisulphite compound with a sufficient amount of a solution of sodium carbonate.

An excess of sulphuric acid beyond the theoretical amount usually accelerates the process of oxidation. Beilstein (Ann. **133**, 4) recommends the use of four times their weight of bichromate for aromatic hydrocarbons. Popow (Ann. **161**, 291) uses bichromate (3 parts), sulphuric acid (1 part), and water (10 parts) for oxidising ketones.

The conversion of alcohols into ketones or aldehydes can be carried out extremely well (Ber. **26**, 822) by Beckmann's method (Ann. **250**, 325). By its use he was able to convert menthol, which is hard to oxidise, into laevo-menthone. A solution of bichromate (60 gr. = 1 mol.) and concentrated sulphuric acid (50 gr. = 2.5 mol.) in water (300 cc.) is cooled to 30°, at which temperature the salt begins to crystallise, and the menthol (45 gr.) is added. The latter becomes black superficially from the formation of a chromium compound. Diligent shaking soon brings the oxidation to completion. The liquid acquires a dark-brown tint and becomes gradually warmer. The menthol becomes first soft and then turns into small crystals of a chromium compound. When the temperature reaches 53° the black chromium compound suddenly breaks up into a brown substance, which soon melts and decomposes into menthone. If the temperature does not reach the necessary height, external heat must be applied. If larger quantities are taken the mass must be correspondingly cooled.

Departing somewhat from the rule in the above examples, it is

frequently necessary to use rather concentrated sulphuric acid. Thus Gräbe and Schultess (Ann. **263**, 10) found that to oxidise thioxanthone with potassium bichromate and sulphuric acid the latter had to contain at least 50 per cent. of H_2SO_4 . The same result was attained easily by using chromic acid in acetic acid solution. The product in either case was benzophenonesulphone—

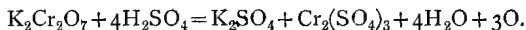


Other acids can be substituted for sulphuric acid. Thus Heinze-mann (Ger. Pat. 4,570) oxidises anthracene to anthraquinone by means of bichromate and hydrochloric acid.

Formerly potassium bichromate and nitric acid were used. For example, Gräbe and Liebermann (Ann. Suppl. **7**, 288) oxidised tetrabromoanthracene (1 part) with potassium chromate (2 parts) and colourless nitric acid of sp. gr. 1·4 (5–6 parts) in a large flask. At first the action was violent and bromine was set free. When this ceased the mixture was diluted with water and the yellow mass of dibromoanthraquinone, which was precipitated, was recrystallised from benzene. This oxidation is much more successful with chromic acid and acetic acid.

A mixture of potassium bichromate and acetic acid sometimes gives quantitative results. For example, Anselm (Ber. **25**, 653) obtained the theoretical amount of naphthalic acid from acenaphthene by this process. He heated acenaphthene (100 gr.) and finely pulverised bichromate (600 gr.) with glacial acetic acid (1,200 cc.) for five hours on the water bath at 80° , and then boiled the mixture, using an inverted condenser, for twenty-five hours more. The product was poured into water, and sufficient sulphuric acid was added to dissolve a chromium compound whose presence otherwise interfered with filtration. The precipitated substance which still remained was collected on a filter and dissolved in boiling dilute caustic soda. This solution was decolourised by boiling with animal charcoal, and the substance was reprecipitated. In place of 140 grams, the theoretical amount, 125 grams of the acid were obtained (cf. § 45).

The oxidising power of these mixtures is calculated on the principle that the CrO_3 is converted into Cr_2O_3 —



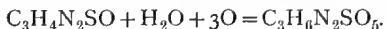
The opinion was once expressed by Fittig (Z. Ch. **1871**, 179) that

ortho-compounds when oxidised were completely decomposed, and failed therefore to yield products similar to those obtained from meta- and para-derivatives. Exceptions to this rule have been observed during succeeding years, so that the law seems not to be so general as he had supposed (Am. Ch. J. **1**, 36).

38. Potassium Chlorate.—This substance has frequently been used as an oxidising agent (M. f. Ch. **4**, 134), and usually in presence of hydrochloric acid. But it must also be remembered that the mixture can give rise to chloro-derivatives.

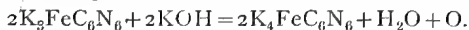
For example, Prager (Ber. **22**, 2,994) dissolved *n*-phenylpropylene- ψ -thiourea (5 gr. = 1 mol.) in a mixture of equal parts of water and crude hydrochloric acid (50 cc.), warmed the mixture slightly, and added potassium chlorate (1 mol.). After the liquid had remained at rest for a considerable time, the product was deposited partly in the form of white needles and partly as a brown resin. The latter gave a quantity of the white crystals on being treated with alcohol.

Andreasch (Ber. **13**, 1,423) covers sulphhydrantoin (5 gr.) with hydrochloric acid of sp. gr. 1.08 (50 cc.), and adds potassium chlorate (4.2 gr.) in five portions. When the action becomes too violent and chlorine is evolved, the mixture must be cooled. If these instructions are observed the body dissolves without any noticeable escape of gas, and the colourless liquid soon becomes turbid from the deposition of a crystalline powder. The sulphhydrantoin is oxidised to carbamidesulphonacetic acid—



The yield of potassium salt averages 70 per cent. of the sulphhydrantoin used, but when the above conditions are not carefully observed the yield is zero, as the reaction takes a different direction.

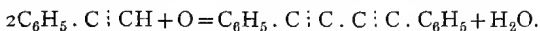
39. Potassium Ferricyanide.—This oxidising agent is used in alkaline solution. It is converted into potassium ferrocyanide according to the equation—



The colour changes during the process from the dark red of the former substance to the light yellow of the latter.

Potassium and sodium hydroxides are the alkalis generally employed, but when these would attack either the substance taken or the product, sodium carbonate may be used.

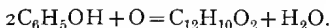
Baeyer (Ber. **15**, 57) employed this oxidising agent for obtaining diphenyldiacetylene from phenylacetylene. He added the copper salt of phenylacetylene (1 mol.) to a solution of ferricyanide (1 mol.) containing caustic potash (1 mol.), and allowed the mixture to remain for twenty-four hours. The precipitate was dried and extracted with alcohol—



In some cases a large excess of the oxidising agent is used. For example, Noyes (Ber. **16**, 53) dissolved potassium ferricyanide (50 gr.) and caustic potash (23 gr.) in warm water (200 cc.), added nitrotoluene (2 gr.) and boiled with reflux condenser for two to three hours. Ortho- and paranitrobenzoic acid were formed. Toluene itself is only oxidised by this agent with difficulty. It is worth noticing that with equal quantities of the oxidising mixture twenty-five times more *p*-nitrotoluene than toluene could be oxidised (Ber. **16**, 2,296).

König (Dissert. Leipzig, 1891) shook a base (2 gr.) with ether (45 cc.), a solution of ferricyanide (7·5 gr.), and caustic potash (13·5 gr.) in water (60 cc.) in a separating funnel. When the ethereal solution was placed in a flask and the ether removed with a current of air, the oxidation product remained behind in crystalline form.

40. Potassium Hydroxide.—The oxidising action of fused potassium hydroxide has been discussed already (cf. Chap. XV.). It may be added here that by its means some syntheses can be effected which are beyond the power of most other oxidising agents (Ber. **21**, 728). Thus it can oxidise phenol, and other similar substances containing a carbon ring, to bodies containing two carbon rings. Thus phenol itself gives diphenol—



41. Potassium Iodate.—This salt has been used as an oxidising agent in solutions containing sulphuric acid.

Warneke (Ar. Pharm. **1888**, 281) dissolved wrightine (10 gr.) in five per cent. sulphuric acid (100 gr.), added a solution of potassium iodate (5 gr.) in water (150 cc.) and set the mixture aside in a dark place for twenty-four hours. The iodine which separated was extracted with chloroform, and ammonia was cautiously added to the colourless liquid. The oxywrightine came out in crystalline form, and the quantity obtained was approximately equal to that of the

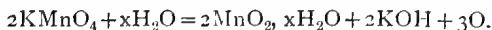
original alkaloid. The preparation of this product by means of other oxidising agents had been attempted in vain.

42. Potassium Manganate.—Baeyer found that this salt was much less active than the permanganate, and could be used for the oxidation of such substances as were over-oxidised by the latter. A solution of the substance is best made by adding a sufficient amount of alcohol to an alkaline solution of permanganate.

Fahlberg and List (Ber. **21**, 243) stated that *o*-sulphaminebenzoic acid was most easily prepared by oxidising *o*-toluenesulphamide with an alkaline solution of potassium manganate. They prepared the oxidising agent by fusing caustic potash (2 parts) with manganese dioxide (1 part) and dissolving the mass in water. The content of manganate is readily ascertainable by titration with oxalic acid. It is advisable to use excess of the manganate solution. The oxidation is accomplished in a few seconds on the water bath, and the excess of manganate is decomposed with alcohol. The solution is filtered from the deposited manganese dioxide, nearly neutralised with acid, concentrated on the water bath, and extracted with ether. By using this process the above observers obtained yields almost equivalent to those theoretically possible.

43. Potassium Permanganate.—In contrast to the manganate, which is seldom employed, the present salt is more frequently used than any other oxidising agent. Its popularity may be explained by the fact that it can be used in neutral, alkaline, or acid solution, and that the termination of the operation is indicated by the disappearance of its very marked colour. Baeyer (Ann. **245**, 146) founded his method of distinguishing between unsaturated acids and saturated acids containing open or closed chains and carboxylic acids of benzene and similar bodies on the precision with which alkaline permanganate acts upon whole classes of organic substances in a perfectly analogous manner.

When used in *neutral solution* the decomposition is in accordance with the equation—

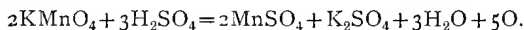


If the caustic potash formed by the action has a disturbing influence, carbon dioxide may be conducted through the liquid while the permanganate solution flows in slowly in a thin stream (see below). The oxidation is often conducted very slowly, and the

addition of permanganate is stopped when it ceases to be decolourised after standing for a considerable time, say twenty-four hours. The solution usually employed contains about 40 grams of the crystallised salt in a litre.

The process of oxidation in *alkaline solution* is exactly similar to that in neutral solution. In both cases the theoretical oxidising power is calculated on the assumption that hydrated manganese dioxide is precipitated.

In working with an *acid solution*, it must be remembered that the metal is dissolved and forms a manganous salt, so that the equation is—



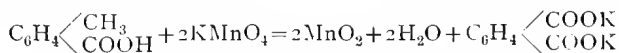
In this case the acid and permanganate are added alternately in small quantities, so that the whole of the acid is not present at one time.

Aromatic sulphides are converted into sulphones by the action of the calculated amount of dry pulverised permanganate in acetic acid solution. An unusual method pursued by Semmler (Ber. **24**, 3,819) was to pulverise the permanganate, pour melted myristicine over it, repulverise the mixture when it solidified, and throw it into boiling water. When the water cooled myristicinic aldehyde, a substance which could be obtained by no other method, was deposited. On adding phosphoric acid to the mother-liquor, myristicinic acid was precipitated.

The activity of the permanganate naturally varies with the conditions under which it is applied. For example, Fahlberg and List (Ber. **21**, 243) found that when *o*-toluenesulphamide was oxidised by it in neutral solution, benzoylsulphinide was formed, but as the amount of free alkali increased with addition of the permanganate, more and more *o*-sulphaminebenzoic acid was produced. The latter was formed exclusively when a strongly alkaline solution was used. But when hydrochloric acid was present or carbon dioxide was conducted through the liquid during the operation, the action was very rapid, and more than twice as much permanganate was used as would suffice to oxidise the methyl group. The solution was found on examination to contain *o*-sulphobenzoate and nitrate of potassium. Using Schlösing's method they were able to show that the whole of the nitrogen of the toluenesulphamide had been oxidised to nitric acid.

Weith (Ber. **7**, 1,058) dissolved pure orthotoluic acid in caustic

soda, and added to the solution rather more permanganate than the equation—



requires. After heating the mixture for ten hours on the water bath the oxidation was complete. The faintly green solution was decolourised with alcohol and filtered, and the phthalic acid was precipitated with hydrochloric acid.

Luff (Ber. **22**, 297) dissolved nitroxycinnamic acid, m.p. 218° (2 gr.), in soda, warmed the solution on the water bath, and added the solution of permanganate (5 gr.) slowly. After heating the solution for a long time, it was acidified, the manganese dioxide was dissolved by adding sodium sulphite, and the clear solution was extracted with ether. Nitroxybenzoic acid was obtained.

Bacyer (Ann. **245**, 139) oxidised the diacetate of *p*-xylylene alcohol, $\text{C}_6\text{H}_4(\text{CH}_2 \cdot \text{C}_2\text{H}_3\text{O}_2)_2$, by warming it in a large basin on the water bath along with water (1,000 cc.) and caustic soda of sp. gr. 1.22 (500 gr.). A 10 per cent. solution of permanganate (4.5 l.) was gradually added. Finally, a further quantity of permanganate was added, if necessary, until the solution became permanently violet, and retained this colour even after three hours' heating. After the excess of permanganate had been decomposed the liquid was filtered through cloth to remove the dioxide. The latter, being very finely divided, had to be washed with water containing soda to prevent any of the precipitate running through. By adding acid very slowly to the warm solution, terephthalic acid was thrown down in needles. The yield was 125 per cent. of the *p*-xylene originally used.

Reactions of this kind can be carried out quantitatively in very dilute solution. On this fact, for example, Fox and Wanklyn (Z. analyt. Ch. **25**, 587) base a method for the quantitative estimation of glycerol, in which an alkaline solution containing at most 25 per cent. of this alcohol is employed.

The following was a very guarded method of oxidising used by Laves (Ber. **23**, 1,415). He dissolved phenyl trithioformate (5–10 gr.) in benzene, and added gradually to the solution, which was shaken continuously, permanganate solution and enough sulphuric acid to preserve a constant acid reaction. After the operation had occupied about two hours, the action was brought to an end by heating on the water bath, and the excess of permanganate was destroyed with sulphuric acid. The aqueous layer was found

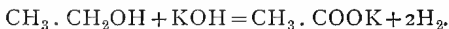
to contain a considerable amount of benzenesulphonic acid. From the dried manganese dioxide a disulphonsulphide was extracted by alcohol. When the process was modified (Ber. **25**, 347) by dissolving the ester in very little benzene and adding a cold mixture of equal parts of 5 per cent. permanganate and 2 per cent. sulphuric acid until it was no longer decolourised, the mixture being shaken constantly during the gradual addition of the liquid, it was found that, on dissolving the manganese dioxide with sulphurous acid, the evaporated benzene solution gave twice as much as before of that oxidation product which was insoluble in water.

It is often observed that the action of the permanganate is very violent. For example, Cottau (Ber. **18**, 376*c*) found that the action on an aqueous solution of chloral hydrate took place in two stages. In the first phase, the chloral was completely decomposed, and chlorine, oxygen, and carbon dioxide were evolved, and manganese dioxide and potassium manganate were formed. In the second phase, the last product converted the chloral into chloroform, and carbon dioxide and oxygen, without chlorine, were given off.

As has already been mentioned, the small excess of permanganate, which remains after an oxidisation is complete, is decomposed with alcohol or sulphurous acid. Sodium formate may also be used for the purpose.

44. Soda Lime.—After Dumas and Stas (Ann. **35**, 133) had come to the conclusion, on purely theoretical grounds, that when alcohol was converted into acetic acid in presence of alkalis, the acid must owe its formation to the oxygen of the water, they found that soda lime, which they were the first to prepare, was a very suitable alkali for the purpose. They prepared it by raising to a red heat a mixture of equal parts of potassium hydroxide and pulverised caustic lime. This mixture became very hard on cooling, and could then be reduced to powder.

When this mixture is brought in contact with alcohol, addition takes place at once. The excess of the liquid can be expelled on the water bath, and a solid mass containing lime, caustic potash, and alcohol remains. When this solid is heated in a tube without access of air, hydrogen gas is evolved very copiously, and strong acids set acetic acid free from the residue,



Brodie (Ann. **71**, 149) used this process for converting ceryl alcohol into cerotic acid and melissic alcohol into melissic acid.

Hell (Ann. **223**, 269) then devised a quantitative method, depending on this reaction, for determining the molecular weight and atomicity of the higher fatty alcohols. The quantity of hydrogen evolved evidently depends on the molecular weight of the alcohol

in such a way that the larger the molecular weight is, the less hydrogen will be evolved. Since alcohols and aldehydes containing the same amount of carbon in the molecule produce the same acids when fused with caustic potash, while the former will evolve twice as much hydrogen in the process as the latter, the fusion provides a convenient means of deciding to which class an unknown substance belongs. The value of this method depends on the fact that the ordinary ways fail to give precise information when bodies of high molecular weight are in question.

Still later Liebermann (Ber. **20**, 962) found in examining cocerylic alcohol by this process that the oxidation took a very irregular course. He obtained a well characterised acid, however, by using a solution of chromic acid in acetic acid.

45. Sodium Bichromate.—This salt has the great advantage over potassium bichromate that it is much more soluble in water, and it can therefore be used in solution without great dilution being necessary. The potassium salt requires ten times its weight of water at 20°, while the sodium salt requires only from two to three times its weight of the same solvent. The amount of chromic acid in the commercial salt varies, however, and consequently, except where a change of colour gives information as to the progress of the action, the quantity which will be necessary has to be determined by previous analysis.

Kissling (Ch. Z. **1891**, 374) recommends the titration of the salt with a solution of ferrous ammonium sulphate, using potassium ferricyanide as indicator. A drop of the solution is brought in contact with a drop of the indicator from time to time. The content of sodium bichromate varies from 88 to 92 per cent., but may be as low as 84 per cent.

In most cases the mixture used in oxidation has a concentration similar to that given for potassium bichromate. It is often found that a large amount of sulphuric acid cannot be added on account of its action on the substance to be oxidised. It is therefore usual to add only sufficient acid to decompose the bichromate.

Nietzki (Ber. **19**, 1,468) gives the following method of oxidising aniline to quinone, to take the place of his earlier process in which potassium bichromate (Ann. **215**, 127) was used.

A mixture of aniline (1 part), water (25 parts), and sulphuric acid (8 parts) is well cooled, and a concentrated solution of sodium bichromate is allowed to flow in. The liquid soon becomes dark-

green, and, towards the end of the action, black. When more bichromate is added, the most of the precipitate disappears, and a brown turbid liquid remains, in which quinone and quinol are suspended. The latter can be oxidised, by further additions of bichromate, to quinone.

To obtain quinol, sulphurous acid is led through the mass until the whole has been reduced, and the filtered liquid is extracted with ether. The direct extraction of the quinone is almost impossible, on account of the formation of an emulsion. The quinol is dissolved in the minimum amount of water, and twice its weight of sulphuric acid is added. The mixture is then cooled, and a solution of sodium bichromate is added until the quinhydrone, which is at first formed, is all converted into pure yellow quinone. It is removed by filtration and the part dissolved is extracted with ether. The yield of quinone from quinol is equal to that theoretically possible.

When the temperature of the mixture was kept at $5-10^{\circ}$, Nietzki obtained yields up to 85 per cent. of crude quinol. Later Schniter (Ber. **20**, 2,283) succeeded in increasing the yield by a slight change in the conditions. He added the oxidising agent, which in this case was potassium bichromate, in two portions, allowing a period of from twelve to twenty-four hours to elapse between the addition of the first third and the last two-thirds of the salt. From 20 grams of aniline he obtained 19 grams of quinone, or 86 per cent. of the theoretically possible amount. Thus quinone, which, before Nietzki discovered the method of preparing it from aniline, was quoted at a price almost equal to that of gold itself (Ber. **10**, 1,934), has now become one of the substances which are easily prepared in large quantities.

According to Hesse (Ann. **200**, 240), quinone is best crystallised from petroleum ether. Sarauw (Ann. **209**, 99) states that the hot saturated solution in petroleum ether, after being filtered, should not be allowed to become completely cold, as the substance last deposited is somewhat impure. The warm mother-liquor should be poured off as soon as a slight cooling has led to the deposit a large proportion of the crystalline quinone.

Under potassium bichromate, a method of converting acenaphthene quantitatively into naphthalic acid was described. Even here the sodium salt may be used with advantage, as the oxidation is more expeditious and the product can be obtained directly in a purer condition. The yields are only slightly smaller—25 grams of the hydrocarbon give 28-29 grams of the

anhydride of the acid. Gräbe and Gfeller (Ber. **25**, 653) state however that the oxidation must be conducted at first with caution, as the action is liable to become too intense. The acenaphthene (25 gr.) is dissolved in warm glacial acetic acid (300 cc.). When the solution has cooled to 80° coarsely powdered sodium bichromate (170–175 gr.) is added, at first very cautiously, care being taken that the temperature does not exceed 85°. When the action becomes less violent the bichromate is added more rapidly, and finally the whole is warmed on the water bath. The whole operation, with the quantities given, occupies an hour. The mixture is finally heated, with inverted condenser, in an oil bath for two hours, and then poured into warm water. The granular precipitate is collected on a filter with the help of a filter pump. On warming with 5 per cent. caustic soda (400 cc.) the product dissolves, and any of the unchanged substance which may remain behind is oxidised by a repetition of the same process.

It is usually stated that phthalic acid is prepared by oxidising tetrachloronaphthalene with nitric acid. Lüddens (Ch. Z. **1891**, 585) mentions that it is now prepared technically by the oxidation of naphthalene or naphthalenesulphonic acid with sodium bichromate and sulphuric acid.

46. Sodium Nitrite.—Sodium nitrite is not very frequently used as an oxidising agent, but, as Nölting has found, it can occasionally be used very effectively. Nietzki and Steinmann (Ber. **20**, 1,278) employed it in preparing purpurogallin from pyrogallol, and obtained a better yield in this way than by any other process. The solution of pyrogallol was acidified with acetic acid, and sodium nitrite solution was added as long as nitrogen was evolved. The precipitated substance was recrystallised after boiling with animal charcoal.

Some years before this, Bernthsen (Ber. **16**, 1,817) investigated its action on methylhydrophenylacridine. On adding sodium nitrite and hydrochloric acid to an alcoholic solution of the substance, he found that the colour changed at once and methylphenylacridinium hydroxide was isolated by evaporating the alcohol, dissolving the residue in water, and precipitating with caustic alkali. The fact that the methyl group remained intact is unprecedented in the history of oxidation.

V. Pechmann states (Ber. **26**, 1,045) that hydrazones are most easily oxidised to tetrazones by *amyl nitrite* (cf. § 30).

47. Sodium Peroxide.—This substance, which has recently become an article of commerce, has not as yet found very wide application as an oxidising agent in organic chemistry (cf., however, Ber. **26**, 3,083).

48. Silver Acetate.—Tafel (Ber. **25**, 1,621) found in this salt a very useful agent for converting piperidine and hydroquinoline derivatives into the corresponding pyridine and quinoline compounds. Piperidine (2.5 gr.) was dissolved in 10 per cent. acetic acid (25 cc.), and the solution was heated for four hours in a hard glass tube with silver acetate (30 gr.) at 180°. When the tube was opened, carbon dioxide escaped, and the silver acetate was found to have been replaced by a gray spongy mass of silver, while the liquid had become brown. The liquid was filtered, the silver was washed with water, and the filtrate was mixed with much solid caustic potash and distilled. The pyridine which passed over still contained a little piperidine. By a similar process he prepared conyryne from coniine.

49. Silver Nitrate.—This salt was used by Bladin (Ber. **25**, 185) for oxidising ethyldenedicyanphenylhydrazine by dissolving the latter in alcohol and adding a solution of silver nitrate at the ordinary temperature. When the liquid was filtered from precipitated silver, phenylmethylcyantriazol was thrown down by water.

50. Silver Oxide.—Effective oxidation with silver oxide seems only to be possible in alkaline solution. For example, Kiliani (Ber. **16**, 2,415) found that it had very little action on a dilute solution of glycerol, even when the mixture was heated for several days at 60°. On the other hand, large quantities of glycollic acid were obtained in alkaline solution. He added the silver oxide, obtained from silver nitrate (60 gr.), to a solution of 85 per cent. glycerol (10 gr.) in water (200 cc.), with which calcium hydroxide (6 gr.) had been mixed, and warmed the whole slowly to 60° on the water bath. All the oxide was reduced at the end of four hours. Carbon dioxide was conducted through the solution, and the precipitated chalk filtered off. On evaporating the filtrate, glycollate of calcium (4.6 gr.) crystallised out. The yield was relatively very good.

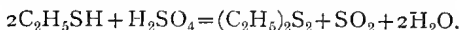
As is well known, ammoniacal silver solutions are the best reagents for recognising aldehydes or converting them into the corresponding acids. The silver is precipitated as metal. Tollens (Ber. **15**, 1,830) states that such a solution is best prepared by mixing a solution of silver nitrate (1 part) in water (10 parts) and of caustic soda (1 part) in water (10 parts), and adding ammonia drop by drop until the silver oxide has dissolved. The solution is preserved in a stoppered bottle, and kept in a dark place. The

ingredients should never be mixed in chance proportions, and care should be taken never to let this solution evaporate, as the fulminate of silver which is deposited may lead to dangerous explosions.

Eichengrün and Einhorn (Ber. **23**, 2,886) found that the following was the only way in which dihydrobenzoic acid could be obtained from the aldehyde. Stronger oxidising agents always gave benzoic acid. Freshly precipitated silver oxide (25 gr.) was dissolved in the quantity of very dilute ammonia which just sufficed for the purpose, a few drops of caustic soda were added, and the solution was warmed on the water bath to 60–70°. The dihydrobenzaldehyde (5 gr.), dissolved in a little alcohol, was allowed to flow in drop by drop. The liquid became dark during the process from the separation of metallic silver. The mixture was warmed and shaken for a short time until a thick mirror of silver had deposited itself on the side of the flask. It was then acidified with hydrochloric acid, and the hydrobenzoic acid was removed from the filtrate by extraction with ether.

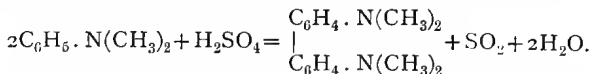
51. Sulphuric Acid.—Both concentrated and fuming sulphuric acids are very useful oxidising agents for substances which are attacked with difficulty, especially as high temperatures can be used without the assistance of sealed tubes.

As early as 1861 Erlenmeyer and Lisenko (Jahresb. **1861**, 590) prepared ethyl disulphide from mercaptan by this method—



Königs (Ber. **12**, 2,342) finally achieved the long sought conversion of piperidine into pyridine by heating piperidine (10 gr.) with excess of sulphuric acid for seven hours at 300°. During the operation a gentle stream of sulphur dioxide was given off, and the liquid became brown, although no carbon was deposited.

Michler and Pattinson (Ber. **14**, 2,162) heated dimethylaniline with three or four times its weight of sulphuric acid for six hours at 180–210°. A continuous stream of sulphur dioxide was evolved, and tetramethylbenzidine was formed—

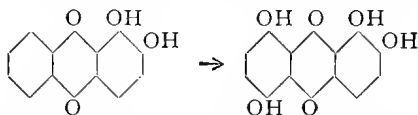


An observation was made by Schmidt (J. pr. Ch. **151**, 238), the importance of which seems to have been realised so far only by

technical chemists. He found that when anthracene derivatives, including even anthraquinone, were treated at a low temperature with large excess of sulphuric acid containing 70-85 per cent. of anhydride, oxidation products alone were obtained, and no sulphonic acids were formed.

For example, he heated one part of dry alizarin (dioxyanthraquinone) with ten or more parts of sulphuric acid containing 70-80 per cent. of SO_3 at $25-30^\circ$ for a period of from one to four days, and then poured the product into ice. An orange-yellow precipitate, insoluble in water, was formed, whose properties agreed with those of the neutral sulphate of a new colouring matter. It could be crystallised under certain conditions. It was soluble in caustic alkalis. When the alkaline solution was acidified a deep brownish-yellow clear liquid resulted, which on boiling deposited a copious precipitate of the final product, alizarin-bordeaux. The yield was almost equal to the theoretical.

The investigations of Gattermann have shown that this substance is a tetroxanthraquinone, and contains no sulphonic acid group. It contains therefore two atoms of oxygen more than the original substance—



When this substance is acted on by sulphuric acid (J. pr. Ch. **151**, 250; cf. also Ber. **24**, 3,067), at 200° , or anthraquinone itself is treated with sulphuric anhydride at 30° , dark-green crystals of hexoxyanthraquinone are obtained. It is evident therefore that under these conditions sulphuric acid always acts as an oxidising agent towards bodies of this class.

52. Tin Tetrachloride.—This substance was used by Poirrier and Chappat (Fr. Pat. 71,970) for the oxidation of methylaniline. They added one part of the former to six parts of a concentrated solution of the latter, and heated the mixture until it became viscous. They precipitated the tin with alkali, and separated the dye by addition of salt.

53. Zinc Permanganate.—Guareschi (Ann. **222**, 305) suspended thioaldehyde (150 gr.) in portions of 25-50 grams in water

(400 cc.), and added zinc permanganate (450 gr.) in water (6 l.). The action was complicated, and the results differed from those obtained by the use of potassium permanganate.

In a few cases oxidation can be combined with condensation (cf. Chap. XII. § 36).

Heusler (Ber. **25**, 1,668) sought to separate the constituents of the tar, obtained by distilling brown coal, by fractional oxidation.

CHAPTER XIX

REDUCTION

1. Reducing Agents.—The following substances have been used as reducing agents¹:—

Aluminium.	Phenylhydrazine.
Ammonia.	Phosphorous acid.
Ammonium sulphide.	Phosphorous iodide.
Chromous chloride.	Phosphorus.
Ferrous chloride.	Potassium arsenite.
Ferrous sulphate.	Potassium hydrosulphide.
Ferrous potassium oxalate.	Potassium hydroxide, alcoholic.
Formaldehyde.	Potassium xanthate.
Grape sugar.	Sodium.
Hydriodic acid.	Sodium amalgam.
Hydrogen sulphide.	Sulphurous acid.
Hydroxylamine.	Tin.
Iron.	Tin bichloride.
Magnesium.	Zinc.
Palladium-hydrogen.	Zinc dust.

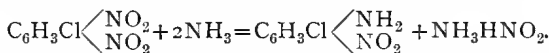
¹ The use of nascent hydrogen produced by electrolysis (Ger. Pat. 21,131) for the reduction of organic compounds seems to have met with no success in the laboratory. For example, Häussermann (Ch. Z. **1893**, 129) states that when nitrobenzene is treated in this way in presence of alcoholic caustic soda hydrazobenzene and benzidine sulphate (yield, together, 60 per cent.) are formed. In presence of dilute sulphuric acid and alcohol benzidine sulphate and azoxybenzene are obtained. Even at a temperature of 60° (Ch. Z. **1893**, 209), only traces of aniline are produced. On the other hand, by using a cathode of zinc in place of platinum, aniline becomes the chief product.

Here, as with oxidation, a better result is sometimes obtainable by substitution of some other chemical change for direct reduction.

As may be seen from some of the examples given below it is sometimes necessary to protect the product of reduction from the oxidising influence of the air. In such cases an atmosphere of carbon dioxide is used, or hydrogen sulphide is conducted through the liquid, or a solution of sodium hyposulphite or of sodium thio-sulphate is added to the mixture. The hyposulphite solution is obtained by adding zinc dust to sodium hydrogen sulphite. In many cases also a layer of ether on the surface of the liquid will be effective.

2. Aluminium.—This metal was used by Curtius and Jay (J. pr. Ch. **147**, 27) instead of zinc, but it did not appear to have any advantages over the commoner metal.

3. Ammonia.—Ammonia has a reducing effect on many nitro-derivatives. For example, Laubenheimer (Ber. **9**, 1,826) found that after a solution of dinitrochlorobenzene, saturated with ammonia, had remained at rest for four days a change had taken place which was represented by the equation—



Six years earlier, however, Clemm (J. pr. Ch. **109**, 170) had shown that, when the substance was heated with strong ammonia at 120° , the reaction took quite a different course.

4. Ammonium Sulphide.—When several nitro-groups are present they may be reduced one after the other by means of ammonium sulphide. Orthonitraniline (Ber. **25**, 987), however, may be boiled for hours with ammonium sulphide without the neighbouring nitro-group being attacked. This was formerly supposed to be the only method by which such results could be obtained, but now other reducing agents are known which act in the same way.

Very often alcoholic solutions of ammonium sulphide are used. They act less energetically than aqueous solutions. For example, Schultze (Ann. **251**, 158) states that *m*-nitrobenzamide is reduced by the latter but not by the former.

Aside from this, however, there are other circumstances which

give the alcoholic solution an advantage. For example, Morgan (Ch. N. **36**, 269) prepared carbostyryl by reducing *o*-nitrocinnamic acid with aqueous ammonium sulphide. Later, Friedländer and Ostermaier (Ber. **14**, 1,916) found that the method was only of practical value when alcohol took the place of water. In Morgan's experiment large quantities of resinous matters were formed so that the yield of carbostyryl was diminished and its purification hindered. By using the ester of the acid and treating it with alcoholic ammonium sulphide the authors avoided the formation of resin entirely. Along with the carbostyryl, however, another substance, oxycarbostyryl, was always formed in greater or less amount. Hardly a trace of it was obtained by Morgan's method. The authors endeavoured in vain, by altering the concentration and quantity of the reducing agent and the duration of the action, to determine exactly what conditions favoured its formation.

The preparation of these two substances is as follows: The *o*-nitrocinnamic ether is heated in portions of thirty or forty grams for several hours with concentrated alcoholic ammonium sulphide in strong soda-water bottles placed in a water bath. When the reduction is complete and the liquid becomes cold, a part of the oxycarbostyryl separates as an ammonium salt in shining plates, and can be collected on a filter. The alcoholic filtrate, which has acquired a brown colour from the separation of sulphur, is then evaporated to dryness, and the residue is extracted with dilute caustic soda. Pure carbostyryl is thrown down by passing carbon dioxide through the alkaline solution, and on subsequently adding sulphuric acid the oxycarbostyryl is precipitated.

Ammonium sulphide also lends itself to the reduction of one of three nitro-groups. Tiemann (Ber. **3**, 218) found that trinitrotoluene could be reduced to dinitrotoluidine by this means. Beilstein (Ber. **13**, 243) found the yield to be so poor that he communicated an improvement on Tiemann's method. He dissolved trinitrotoluene (1 part) in alcohol (2 parts), and added gradually the theoretical amount of hydrogen sulphide (3 mol.) in the form of a concentrated aqueous solution of ammonium sulphide. After each addition of the latter the precipitate was well stirred. The mixture was allowed to rest for a short time, and was finally mixed with water. The precipitate was filtered, washed, and boiled repeatedly with dilute hydrochloric acid as long as ammonia caused any precipitation in the extract. The dinitrotoluidine was purified by recrystallisation.

Bader (Ber. **24**, 1,654) obtained an almost quantitative yield of dinitraniline from trinitrobenzene. He dissolved trinitrobenzene (15 gr.) in absolute alcohol (450 cc.) by boiling in a large flask attached to a condenser till a clear solution resulted. He then allowed a strong solution of ammonium sulphide (90 cc.) to flow drop by drop from a funnel into the boiling liquid. Even after the addition of a few drops of the sulphide the liquid became brown. The boiling was continued for an hour or an hour and a half, and the solution was then poured into two or three litres of ice-cold water, the latter being well stirred during the addition. The dinitraniline separated at once in the form of a yellow flocculent precipitate.

Alcoholic ammonium sulphide is sometimes enclosed in a sealed tube with the substance to be reduced. This method was employed by Schöpf with the reduction of *m*-nitro-*p*-anilidobenzoic acid.

Beilstein and Kurbatow (Ber. **11**, 2,056) attempted to reduce one of the nitro-groups in chlorodinitrobenzene with alcoholic ammonium sulphide. They obtained, however, a substance containing sulphur, through the action of the chlorine atom, instead of chloronitraniline. Further experiment showed them that ammonium sulphide acted as a reducing agent only on substances like symmetrical nitrodichlorobenzene in which the nitro-group had no chloro-group or other nitro-groups as neighbours. In all other cases, the chloro- or nitro-group is exchanged for sulphur or a group containing sulphur.

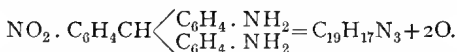
5. Chromous Chloride.—A solution of chromous chloride in glacial acetic acid was used by Gimbel (Ber. **20**, 975) for the reduction of nitrosoanthrone.

6. Ferrous Chloride or Sulphate.—These salts are often used where free hydrogen cannot be employed; as, for example, where the latter might add itself to the substance to be reduced.

Ferrous chloride can be used in the solid form or in aqueous or alcoholic solution (Centralblatt, **1849**, 807).

O. Fischer (Ger. Pat. 16,750) has even found it possible to obtain reduction and oxidation simultaneously in presence of ferrous chloride. Paranitrodiamidotriphenylmethane gives on reduction paralencaniline, which can be oxidised in turn to rosaniline. Instead of conducting the operation in two stages, he converts the substance directly into rosaniline as follows: The paranitrodiamidotriphenylmethane (1 part) is heated with solid ferrous chloride (2 parts) at 160–180° and stirred until a homogeneous fused mass of a bronze colour is obtained. The product is extracted with dilute hydrochloric acid, and the dissolved fuchsine is afterwards

separated from the solution. In this case the ferrous chloride reduces the nitro-group, and simultaneously the methane group is oxidised. The formation of rosaniline is expressed by the equation—



The same reaction can also be carried out with homologues of nitrodiamidotriphenylmethane as well as with a mixture of aniline and toluidine.

Ferrous sulphate is much more frequently employed than ferrous chloride, on account of the fact that its solid form permits of more convenient quantitative use. In applying it for the purpose of reduction, an aqueous solution is added to an alkaline liquid, and the ferrous hydroxide which is precipitated effects the reduction. It is specially useful in the case of unstable substances. The alkalis used are ammonia, baryta water, and caustic soda.

Baeyer and Bloem (Ber. **15**, 2,147) dissolved *o*-nitrophenylpropionic acid in excess of ammonia, and added gradually a saturated solution of ferrous sulphate (10 parts). During the operation the alkalinity of the liquid was maintained by addition of ammonia. The reduction proceeded quickly, and its termination was recognised by the fact that the brownish-black precipitate became reddish-brown in colour.

Sometimes the ferrous sulphate is added to a boiling alkaline solution.

Gnehm (Ber. **17**, 754) suspended nitrodichlorobenzaldehyde (10 gr.) in a solution of ferrous sulphate (100 gr.) in water (1 l.), and added excess of ammonia to the liquid. The amido-compound which was formed was driven over with steam. This substance was little soluble in water, but had the unusual property of dissolving in a solution of sodium bisulphite, from which it could be reprecipitated by acids or alkalis.

The use of baryta water originated with Wöhler (Pogg. Ann. **13**, 448), who reduced picric acid (trinitrophenol), to picramic acid (dinitroamidophenol), in its presence.

Claisen and Thompson (Ber. **12**, 1,946) used the same alkali in reducing nitro-acids as follows: The nitro-acid was dissolved with the calculated amount of barium hydroxide; the necessary quantity of ferrous sulphate was then added to the warm solution, and finally sufficient baryta water was added to precipitate the whole of the iron. The mixture was warmed on the water bath until the

ferrous oxide had acquired the reddish-brown colour of ferric hydroxide. The barium sulphate and ferric oxide were then removed by filtration, the barium in solution was precipitated with carbon dioxide, and the solution, which contained the barium salt of the amido-acid, was concentrated by evaporation. From the warm solution the acid, which in this case was *m*-amidophenylglyoxylic acid (*m*-isatoic acid), was precipitated by adding hydrochloric acid. An excess of the latter had to be carefully avoided, as it formed a soluble hydrochloride with the amido-acid. The authors found that it was best to add a small portion only of the hydrochloric acid at one time, allow the liquid to cool, and remove by filtration the crystalline precipitate, which formed very slowly. This operation was repeated until at length no more crystals could be obtained. The employment of acetic acid, which is generally used for precipitating amido-acids, was here inapplicable because it does not decompose the salts of *m*-isatoic acid.

In separating amido-acids from their hydrochlorides the method of Döbner and v. Miller (Ber. **17**, 939) may be used. The hydrochloride is dissolved in water, and the calculated amount of sodium acetate or carbonate is added. If the acid is insoluble, it is at once precipitated, or at all events crystallises out on standing. If it is soluble, the solution is evaporated on the water bath, and the acid or its sodium salt is extracted from the residue with alcohol.

Attempts to use ferrous sulphate in acid solution—as, for example, with concentrated sulphuric acid—have been unsuccessful.

7. Ferrous Potassium Oxalate.—Eder (M. f. Ch. **1**, 137) states that ferrous potassium oxalate is a much more efficient reducing agent than any other organic or inorganic salt of iron. He finds that its action is similar to that of ferrous hydroxide in alkaline solution, ammoniacal cuprous chloride, or an alkaline solution of pyrogalllic acid. The reducing power manifests itself, not only in faintly alkaline and neutral solutions, but also in those which are slightly acid. The addition of too much acid, however, causes deposit of yellow ferrous oxalate.

8. Formaldehyde.—This substance is used in the reduction of azo-dyes formed from nitramines (Ger. Pat. 62,352).

9. Grape Sugar.—Grape sugar and milk sugar are used for reducing purposes in 10 per cent. solution in water. This is added

to an alkaline solution of the substance and the mixture is boiled. This process is frequently used in the reduction of substances which form dyes.

10. Hydriodic Acid.—The very powerful reducing action of hydriodic acid on organic bodies was discovered by Berthelot (Bull. Ch. [2] 7, 53, and J. pr. Ch. 104, 103).

Mendelejeff (Principles of Chem. I., p. 500) gives the strength and specific gravity of hydriodic acid as follows:—

Sp. Gr.	Content of HI.	Sp. Gr.	Content of HI.
1·075 . . .	10 %	1·399 . . .	40 %
1·164 . . .	20 %	1·567 . . .	50 %
1·267 . . .	30 %	1·769 . . .	60 %

The strongest acid preparable by distillation boils at 127°, contains 57·57 per cent. of hydriodic acid, and has a specific gravity of 1·67.

The ease with which it decomposes into hydrogen and iodine accounts for its reducing power. It is used in aqueous solution with or without phosphorus, and in acetic acid solution.

Berthelot, who applied it in absence of phosphorus, states that it reduces every organic substance to the hydrocarbon containing the same amount of carbon and the maximum amount of hydrogen in the molecule. According to him it can be applied to all compounds from fatty alcohols and acids to aromatic compounds and from the nearly saturated ethylene derivatives to those in which all the hydrogen has been replaced by chlorine. By its means hydrogen can be added to amides and even to cyanogen (cf. however § 23, p. 307).

His method consisted in heating the substance with a great excess of strong hydriodic acid (sp. gr. 2) for ten hours at 275°. He estimated that a pressure of a hundred atmospheres was reached under these circumstances. For aromatic bodies he sometimes used as much as one hundred times their weight of the acid.

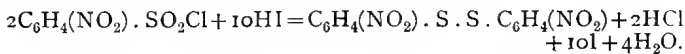
In this way he reduced ethyl iodide and ethyl alcohol to ethane, glycerol to propane, and thought he had reduced benzene to the normal hydrocarbon, C_6H_{14} .¹ Methylamine gave methane and ammonia; aniline, benzene and ammonia, and so forth.

Baeyer (Ber. 19, 1,806) prepared hexahydroterephthalic acid by heating tetrahydroterephthalic acid for six hours at 240° with

¹ These experiments were carried out in 1867–68.

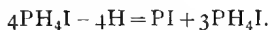
hydriodic acid of 127° boiling-point. The contents of the tube were decolourised with sulphurous acid, and the precipitated acid was dissolved in soda, reprecipitated, and recrystallised from hot water.

A very extraordinary and entirely unexpected action of hydriodic acid was discovered by Eckbom (Ber. **24**, 337). He found that, when *m*-nitrobenzenesulphonic chloride was dissolved in acetic acid, hydriodic acid of sp. gr. 1.5 was added, and the mixture was warmed on the water bath for a short time, the sulpho-group was completely reduced, while the nitro-group remained unattacked. The product was *m*-dinitrodiphenyldisulphine.



Kolbe (Ann. **118**, 122) had found as early as 1861 that benzene derivatives, when treated with sodium amalgam, have the power of taking up hydrogen. After him other observers noticed the same fact, but it was always found that not more than six hydrogen atoms could be added, and the compounds formed had a marked tendency to turn into benzene derivatives again. Those hydrogenated compounds remained difficult to prepare until Baeyer (Ber. **25**, 1,037) showed how they could be made synthetically of almost any desired type out of substances with simple carbon chains (§ 24).

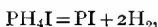
Kolbe's communication induced Baeyer (Ann. **155**, 267) to test Berthelot's results, soon after their publication, under conditions which he expected would be still more favourable to reduction. In Berthelot's process iodine was set free and could not at all assist the reduction by its presence, and furthermore water was present and must have somewhat hindered the action even when the most concentrated acid was used. Both of these substances could be eliminated however by using phosphonium iodide. Any iodine, which was set free by the decomposition of hydriodic acid, would react with the phosphine, as Hofmann had shown, to form iodide of phosphorus, and phosphonium iodide would be reproduced. When the hydriodic acid of this new phosphonium iodide had been in turn decomposed, the same action would again take place until all was converted into iodide of phosphorus and phosphonium iodide, in accordance with the equation—



Although the action followed the expected course, the reducing

power of this combination was found to be much less than that of hydriodic acid itself. Still Baeyer found the reagent valuable as it reduced hydrocarbons to exactly the same extent as sodium amalgam reduced acids.

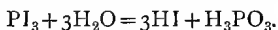
In heating hydrocarbons with phosphonium iodide thick-walled rather narrow tubes must be chosen, as the pressure is sometimes considerable. The weighed quantity of hydriodic acid is first placed in the tube, the hydrocarbon is poured upon it, and finally the air is displaced by carbon dioxide before the tube is sealed up. If the latter precaution is not observed, an explosion may occur from the combustion of the phosphine when heat is applied. When the reduction is complete long red needles are observed in the tube, which probably have the composition PI. This decomposition sometimes takes place without any reduction occurring. The action then follows the equation—



and a very powerful pressure is manifest when the tube is opened.

The object which Baeyer sought to attain, the removal of the iodine, can be accomplished by adding phosphorus. The idea originated with Lautemann (*Ann.* **125**, 9), and with its adoption the method became quite generally applicable, since now the formation of unwelcome by-products containing iodine was reduced to a minimum.

The free phosphorus unites at once with the iodine to form phosphorus iodide, which in turn reacts with water to form hydriodic acid and phosphorus acid—



Still, in the heat, some by-products arise (*C. R.* **91**, 883), and their formation interferes slightly with the course of this theoretically beautiful reaction. Thus when phosphorus and hydriodic acid are heated at 160° , phosphonium iodide is produced.

Yellow and red phosphorus are both used. With the former, reductions can be carried out by simply boiling the substance with strong hydriodic acid in a vessel attached to an inverted condenser. The escaping gaseous acid is caught in water. Even red phosphorus may be used in this way. For example, Liebermann and Topf (*Ber* **9**, 1,201) obtained dihydroanthracene by boiling hydriodic acid (80 gr.) and yellow phosphorus (6 gr.) with anthraquinone (20 gr.) for an hour. Later, however (*Ber.* **20**, 1,854), they found that red phosphorus produced the same result.

Baeyer (*Ber.* **5**, 1,095) connected a flask of one litre capacity

with a wide condenser placed vertically. The upper end of the condenser tube was fitted with a T-tube, through one limb of which pieces of phosphorus could be introduced, while the other served for the escape of hydriodic acid. In the flask hydriodic acid, boiling at 127° (200 gr.), and iodoform (50 gr.) were placed. The mixture was heated to boiling, and small pieces of phosphorus were thrown in until the liquid ceased to become brown even on prolonged boiling. Then further portions of iodoform (100 gr.) and the necessary amounts of phosphorus were added alternately with the same precautions. The iodoform, CHI_3 , was reduced to methylene iodide, CH_2I_2 , which was separated by distillation.

Fischer (Ber. **24**, 1,844) heated trioxylglutaric acid (1 part) with concentrated hydriodic acid (10 parts) and red phosphorus ($\frac{1}{2}$ part) for four hours, in a flask attached to a reflux condenser, diluted the product with water, and removed the hydriodic acid with silver oxide. The warm, colourless filtrate was then freed from silver with hydrochloric acid, and evaporated to a syrupy consistency. This residue solidified to a mass of glutaric acid on cooling. From mannose carboxylic acid (Ber. **22**, 372) he obtained heptylic acid by boiling its barium salt (35 gr.) with hydriodic acid, boiling at 127° (250 gr.), and red phosphorus (10 gr.) for five hours. The dark solution was diluted with water, and the oil which separated was extracted with ether. The extract was shaken with mercury to remove free iodine, and evaporated. The oil which remained (27 gr.) contained much iodine in combination. To decompose the iodine compounds, dilute sulphuric acid was added, and zinc dust was thrown in in small portions. After the mixture had remained at the ordinary temperature for twelve hours, it was distilled in a current of steam. Heptylic acid passed over, and was purified by conversion into the barium salt.

Energetic reduction is attained with this method, as with Berthelot's, by heating in sealed tubes. The amount of hydriodic acid used does not require to be great. Grabe (Ann. **163**, 352) states that it suffices to take such a quantity that the water contained in it is enough to convert the separated iodine and the phosphorus into hydriodic acid and phosphorous acid. In preparing carbazoline,

$\text{C}_{12}\text{H}_{13}\text{N}$, he took carbazol, $\left. \begin{array}{l} \text{C}_6\text{H}_4 \\ | \\ \text{C}_6\text{H}_4 \end{array} \right\} \text{NH}$ (6 gr.), phosphorus (2 gr.), and hydriodic acid (7–8 gr.). He recommends the use of hard glass tubes for such purposes.

Some recent work of Lucas (Ber. **21**, 2,510) has shown however that the maximum reduction of aromatic hydrocarbons can only be reached by using a large excess of the reducing agent and a sufficiently high temperature. Thus he heated anthracene (1·5 gr.) in a sealed tube with red phosphorus (1·5 gr.) and hydriodic acid of sp. gr. 1·7 (8 gr.) for twelve hours at 250°, and obtained in this way the hydrocarbon, $C_{14}H_{24}$. Gräbe reached only $C_{14}H_{16}$.

Chrysene was supposed to be irreducible with hydriodic acid and phosphorus, because too little of the latter had been used. But Liebermann and Spiegel (Ber. **22**, 135, and **23**, 1,143) obtained perhydrochrysene by heating chrysene (1 part) with red phosphorus (1 part) and hydriodic acid of sp. gr. 1·7 (5 parts) for sixteen hours at 250–260°.

Krafft (Ber. **15**, 1,687) has found that the higher fatty acids, from nonylic acid upwards, can be reduced by this method to normal hydrocarbons. He charged strong tubes of hard glass with the fatty acid (2–4 gr.), hydriodic acid of sp. gr. 1·7 (3–4 gr.), and red phosphorus (1·3–1·4 gr.) and heated them at first to 210–240°. These quantities being insufficient for completing the reduction, the exposure to the above heat was limited to a short time lest the iodine set free should decompose the product. This heating was repeated two or three times, and between each heating the tube was opened and a little phosphorus was added. At the third opening or so, an equal amount of water was added from a burette along with the phosphorus, so as to supply a sufficient quantity of this liquid to decompose the phosphorous iodide formed, and thus regenerate the hydriodic acid. At the termination of the operation the hydrocarbon was usually found floating upon the rest of the contents of the tube, and could be separated from them mechanically. In the contrary case, water was added to effect the separation. The products could also be extracted with ether or other solvents.

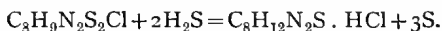
Claus (J. pr. Ch. **153**, 380) reduced mixed fatty and aromatic ketones to hydrocarbons by stirring one molecular proportion of the ketone with one third of its weight of water and an equal weight of red phosphorus, and then adding iodine (4–5 mol.) to the warm mixture. After the whole had been heated for eight days in an open flask with the naked flame, a few drops of water being added if necessary, the brown oily product was distilled with a current of steam. The distillate was extracted with ether. The extract was dried and deprived of free iodine with sodium, and finally the ether was evaporated and the residue distilled over sodium. In this way hydrocarbons of constant boiling-point were obtained, and the yields were from 20 to 25 per cent. (minimum 15 per cent.) of the ketone used. Metamethyl-*p*-ethyltoluene, for example, was prepared in this way from *m*-xyllylmethylketone.

11. Hydrogen Sulphide.—Organic bodies are reduced by hydrogen sulphide, but it acts with difficulty in neutral or acid solution. In

the latter case reduction may be possible if the reagent is applied in the nascent condition, as, for example, by adding zinc, barium, or calcium sulphide to an acid solution of the reducible substance.

Merz and Weith state also that the action is assisted by the presence of finely divided copper.

Bernthsen mentions (Ann. **251**, 23) that methylene red, which is easily reducible with zinc and hydrochloric acid and by stannous chloride and hydrochloric acid, is also reduced by hydrogen sulphide—



Although seldom thus employed, it is an almost indispensable reducing agent in alkaline solution. Its action depends on the fact that its hydrogen unites with oxygen to form water, and the sulphur is deposited or dissolves in excess of the alkaline sulphide. When an ammoniacal solution is used, the excess of the reducing agent can finally be removed by prolonged boiling with water.

The operation usually consists in adding ammonia to the liquid to be reduced and saturating it with hydrogen sulphide. If necessary, the addition of ammonia can be repeated, and more hydrogen sulphide led into the mixture.

Zinin (Ann. **44**, 283) first reduced a nitro-group to an amido-group by this method, by acting with ammonium sulphide on nitrobenzene. This was the first occasion on which a base containing nitrogen had been prepared synthetically from a substance free from nitrogen (benzene), and attracted much attention at the time, as it marked a step in the direction of the artificial preparation of alkaloids.

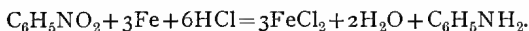
12. Hydroxylamine.—Free hydroxylamine has the power of reducing quinones to quinols. Still, on the whole, its reducing power towards organic bodies is very small. For example, Böniger (Ber. **21**, 1,762) made many experiments with it, all of which failed. This is the more extraordinary, as the powerful reducing action, which it shows in alkaline solution, has led to its very wide application in photography. Silver is instantly precipitated from its solutions in metallic form, and when no other noble metal is present, this is probably the most convenient way of quickly preparing pure silver.

13. Iron.—Metallic iron is often used as a reducing agent, as well as the salts which have been mentioned already.

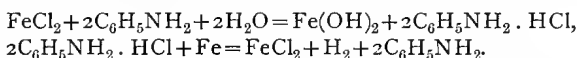
Schmidt and Schultz (Ann. **207**, 329) distilled azoxybenzene (60 gr.) with three times its weight of iron filings, and not a trace of the unchanged substance passed over. The chief product was azobenzene (72.5 per cent.) with aniline and a small amount of carbonised material.

Iron is seldom employed in this way, however, as zinc dust is more effective, but in presence of acids it is very frequently used.

For example, iron and hydrochloric acid is an excellent reducing agent. In this case the extraordinary fact is sometimes observed that much less hydrochloric acid is required than the simplest equation representing the action seems to require. Thus for nitrobenzene, the amount required is represented by the equation—



This peculiarity is explicable as follows: The aniline which is formed decomposes the ferrous or ferric chloride in presence of water giving ferrous or ferric hydroxide and aniline hydrochloride, and the latter is in turn decomposed by the excess of free iron into ferrous chloride, aniline, and hydrogen. The last reduces a further portion of the nitrobenzene, while the ferrous chloride goes through the same transformation once more. The following equations represent these changes—



In the laboratory, iron filings and acetic acid are generally used, and in fact this is the original form in which the method was suggested by Béchamp (Ann. **92**, 401). When the solution is boiled after the reduction is complete, the acetate of iron is decomposed, and finally little or no iron remains in solution. This property gives the method an advantage over others in which a complicated process is necessary for the final removal of the metal.

In working on a small scale, also, very little acetic acid need be used. This renders the method applicable to substances in whose case, for example, there would be danger of saponification by excess of hydrochloric acid.

Thus with *p*-nitracetanilide, tin and hydrochloric acid cannot be used as the hydrochloric acid splits off the acetyl group. This attempt having failed in the hands of Hobrecker (Ber. **5**, 920), Nietzki (Ber. **17**, 343) employed iron and acetic acid. Amido-acetanilide was easily formed, and was extracted from the product

with hot water. It is best to add soda to faint alkaline reaction, and then, all the iron having been precipitated as carbonate, to boil with water.

Lachowitz (Ber. **17**, 1,162) finds also that iron and acetic acid is the best reducing agent for the successive removal of chlorine atoms from chloroketones. His investigations show that no action takes place in the cold. The temperature must first be raised to a definite point before the evolution of hydrogen begins, and the action is more energetic the higher the temperature. The activity of other reducing agents, such as zinc and hydrochloric acid in alcoholic solution, although apparently less is really greater since they remove several chlorine atoms immediately even in the cold.

In particular the examination of dichlorophenanthrone showed that one chlorine atom was replaced at a temperature not exceeding 100° . Under these conditions the monochloro-product is obtained pure and free from results of further reduction. Only when the action has continued for a long time is a part of the monochlorophenanthrone reduced to phenanthrone. This more extensive reduction occurs completely when the temperature is raised from 100° to 110° .

The removal of one of the atoms of chlorine from dichlorobenzil was achieved in the same way.

In the applications of iron for the purpose of reduction which have been thus far described, the action is due to the hydrogen gas which is set free. If the observer wishes to ascertain whether all the hydrogen produced is being used for reduction, the apparatus is filled with carbon dioxide and a stream of the gas is kept up during the action. If the whole of the escaping gas is absorbed by caustic potash, the absence of free hydrogen is proved.

The use of nascent hydrogen in neutral solutions will be described under zinc.

14. Magnesium.—This metal, which is obtainable in the forms of powder and ribbon, has been little used hitherto for the reduction of organic bodies. Baeyer (Ber. **2**, 99) experimented on its action upon acid chlorides. He dissolved the latter, for the purpose, in glacial acetic acid, or suspended them in it. Phthalyl chloride gave phthalic aldehyde.

15. Palladium-hydrogen.—Saytzeff's work (J. pr. Ch. **114**, 128) has shown the great reducing power of palladium charged

with hydrogen. For example, he converted nitrobenzene into aniline by its agency. The method is very inconvenient however.

16. Phenylhydrazine.—The reducing power of this substance was first recognised by Baeyer. Haller (Ber. **18**, 92) reduced pseudocumidine to pseudocumene by its agency. Zincke (Ber. **18**, 787) converted quinone into quinol. Merz and Ris (Ber. **19**, 1,754) noticed, in connection with attempts to make *o*-nitraniline (cf. Ber. **25**, 985), which was then difficult to prepare, more easily accessible, that both the ortho- and para-compounds reacted energetically with phenylhydrazine. Following up this observation, Barr found (Ber. **20**, 1,498) that when nitrophenol was warmed with twice the calculated quantity of phenylhydrazine (2 mol.) diluted with xylene, gas was rapidly evolved, and, on cooling, the mixture deposited crystals of amidophenol. The nitro-group had therefore been reduced to the amido-group.

Seidel (Ber. **23**, 186) found that the ordinary reducing agents had hardly any reducing action on the dye, $C_{18}H_{12}N_2O_2$. But when it was heated to 120° with a solution of phenylhydrazine in xylene, an energetic liberation of nitrogen took place, and soon a substance crystallising in colourless plates was deposited. The phenylhydrazine was broken up quantitatively into benzene, nitrogen, and hydrogen, and the last added itself to the dye forming the leuco base, $C_{18}H_{14}N_2O_2$. Neither aniline nor ammonia was formed.

Phenylhydrazine may be applicable in many other cases, as its power of giving hydrogen at rather high temperatures permits its use in open vessels.

17. Phosphorous Acid.—This reagent seems to possess no special advantages as a reducing agent, and it has seldom been used in this capacity.

18. Phosphorous Iodide.—Phosphorous iodide may be used instead of the mixture of red phosphorus and iodine or hydriodic acid mentioned above. If its employment is desired, it may be prepared according to Annaheim's directions (Ann. **172**, 51). He dissolved the iodine (60 gr.) in a little carbon disulphide, and added phosphorus (8 gr.) in small pieces at a time. Then he evaporated the solvent rapidly on the water bath, and removed the last traces by warming in a current of dry air.

A substance to be reduced, such as dry diamidomethoxysulpho-

benzide (4 gr.), was placed on the iodide, and they were covered with boiling water (30-50 cc.). An energetic emission of gas began at once, and streams of hydriodic acid were evolved. The mass became fluid, and the action seemed to be complete at the end of a few minutes. In this particular case, however, the original substance was recovered unchanged.

19. Phosphorus.—Purpurin (trioxanthraquinone) is converted into purpuroxanthin (metadioxyanthraquinone) (Ann. Ch. Ph. [5], 18, 224) by the action of phosphorus and caustic soda.

20. Potassium Arsenite.—A solution of arsenious acid in potassium hydroxide was used by Williams (Ann. 102, 127) for the conversion of nitrobenzene into aniline. He digested the nitrobenzene with the solution for some time, and then isolated the aniline by distillation.

21. Potassium Hydrosulphide.—Potassium or sodium hydrosulphide may be used exactly like ammonium sulphide. They have the disadvantage that they cannot be removed by evaporation.

22. Alcoholic Potassium Hydroxide.—Alcoholic caustic potash or soda¹ is used almost exclusively for the reduction of nitro-bodies to azoxy-derivatives. They act consequently like sodium amalgam, the nitro-group being reduced through its oxygen oxidising the alcohol. For example, nitrobenzene (1 part) is dissolved in strong alcohol (5-6 parts) and first warmed and finally boiled with solid caustic soda (1 part). The alcohol is distilled off until the residue separates into two layers. The upper brown layer is washed with water until it solidifies to a crystalline mass. Pure azoxybenzene is obtained from this by recrystallisation. The method was devised by Zinin (cf. p. 304), and the yield may reach 40 per cent. of the nitrobenzene used.

Buchka and Schachtbeck (Ber. 22, 835) employed methyl alcohol. In preparing *m*-azoxytoluene, *m*-nitrotoluene (10 gr.) was heated in a flask attached to a condenser with caustic soda (10 gr.) dissolved in methyl alcohol (90 gr.) for about six hours on the water bath. The alcohol was distilled off, and the unchanged nitrotoluene was driven over with steam. The oil which remained was

¹ Very strong solutions of caustic potash in methyl or ethyl alcohol are best prepared by mixing a very concentrated aqueous solution with the alcohols.

extracted with ether, and when this was allowed to evaporate a crystalline residuc remained.

23. Sodium.—Both sodium and sodium amalgam are in very frequent use on account of their great reducing power and the ease with which they can be applied.

The sodium is usually employed in the form of thin discs, although this way of using it has some disadvantages, especially when the surface tends to become covered with an insoluble layer which hinders the action of the parts concealed.

Hofmann (Ber. **7**, 534) introduced the use of a press which supplies it in the form of wire. Brühl (Ber. **24**, 3,384) makes the remark that the metal for producing thin sodium or potassium wire should be purified by fusion under toluene. The wire he used had a diameter of .2 mm. If the metal is not purified in this way the press may easily become stopped up, and in the case of potassium dangerous explosions take place. The metal which has been once fused under toluene so that it flows to a clean liquid metallic mass is sufficiently pure for all purposes. It should be preserved under light petroleum rather than heavy petroleum or toluene. In the former the metals, especially sodium, can be kept almost indefinitely, and may be used directly without being scraped.

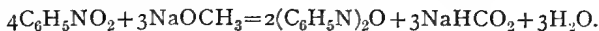
The metals may be obtained in a finely divided state, without the intervention of any machine, as follows : The sodium is covered with petroleum, and heated to about 120°. The flask is corked, well shaken, and, the cork having been removed, is then set aside till cold, in a place where it will not be disturbed. The metal, in cooling, retains its fine granular form. If the temperature exceeds 120° the metal cakes together again on cooling. Levy and Andreocci (Ber. **21**, 1,464), state that when melted paraffin is used in place of petroleum, the metal obtained is still more finely divided. In this case after the shaking the paraffin is poured off, and the remainder washed out with petroleum ether at 50°. They state that the metal is best kept under the same liquid, so that it can be rapidly dried before use.

When considerable quantities of sodium have been used, the addition of water to remove any excess of the metal which may remain is attended with the danger of violent explosion. It is preferable, when the amount of sodium remaining must be small, to add powdered ice. In the contrary case, the flask should be broken, if it cannot be emptied otherwise.

The sodium is allowed to act both on aqueous, alcoholic, and ethereal solutions. To hasten its action the sodium hydroxide which is formed is partially neutralised with acids from time to time, care being taken that the liquid does not actually become acid.

Sometimes the presence of caustic soda is harmful, and yet the liquid may not be rendered acid with a strong acid even temporarily. In such cases an amount of sodium bicarbonate sufficient to neutralise the caustic soda may be added at the beginning.

Klinger (Ber. **15**, 866) has found that a solution of sodium in methyl alcohol, as distinct from ethyl alcohol, is very suitable for the reduction of nitro-bodies to azo-bodies.¹ He used sodium (10 parts) dissolved in methyl alcohol (250 parts), added pure nitrobenzene (30 parts), and boiled the mixture on the water bath for five or six hours in a flask attached to a condenser. The liquid became reddish-brown in colour and remained clear. When the methyl alcohol was distilled off the colour became lighter, crystals of sodium formate separated, and finally a light yellow mass saturated with oil remained behind. On treating this with water, he found that light yellow liquid azoxybenzene, which soon solidified, was deposited. The yield was copious. The action was represented by the equation—



When *p*- and *o*-nitrotoluene were used, no azoxytoluene was obtained.

The reducing action of sodium on solutions in *ethyl alcohol* is best brought into play by adding the metal to the boiling solution. This method was probably first used by Baeyer (Ber. **12**, 459) in the reduction of dichloroindole. Using the same method Wischnegradsky (Ber. **13**, 2,401) prepared hexahydroethylpyridine from ethylpyridine.

Ladenburg (Ann. **247**, 51 and 80), who adopted the method on account of its usefulness, states that it is a point of importance to use as small an excess as possible of absolute alcohol, and to keep the temperature at the boiling-point of the solution.

In converting pyridine into piperidine, he dissolved the pyridine (20 gr.) in absolute alcohol (150 gr.) in a flask attached to a con-

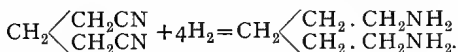
¹ Cf. Witt's use of an alkaline solution of stannous hydroxide for the same purpose (p. 320).

denser, and warmed the solution on the water bath. He then added, not too slowly, the required amount of sodium (75 gr.), which had previously been cut into small pieces and preserved in dry ether. When the action became slow or sodium ethylate separated he added more alcohol, and in general hastened the reduction as much as possible.

When all the sodium was dissolved he allowed the solution to cool, added an equal bulk of water, and distilled the mixture cautiously on the water bath. The piperidine passed over almost entirely with the alcohol. After neutralising with hydrochloric acid the distillate was evaporated to dryness. The yield was practically quantitative.

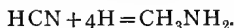
In reducing α -lutidylalkine (Ber. **24**, 1,674), $C_6H_4(CH_2 \cdot CH_2 \cdot CH_2OH)N$ (13 gr.), the base was dissolved in hot absolute alcohol (130 gr.), and the solution was poured on to sodium (50 gr.) which was contained in a large flask attached to a condenser and was warmed on the water bath. As soon as the action became slower more hot absolute alcohol was added. By adding water, extracting with ether, and evaporating the extract, he obtained a base containing six additional atoms of hydrogen, $C_6H_9(CH_2 \cdot CH_2 \cdot CH_2OH)NH$, and having the composition of conhydrine.

He dissolved trimethylene cyanide in eight times its weight of absolute alcohol, added gradually 4 parts of sodium, taking care to exclude moisture, and so obtained pentamethylenediamine—



Pentamethylenediamine, whose preparation by Ladenburg's method is extremely easy, had previously (Ber. **16**, 1,151) been obtained in traces only by the use of other reducing agents.

It may be mentioned that the first reduction of cyanides to amides by means of nascent hydrogen was accomplished by Mendius (Ann. **121**, 129). He prepared methylamine from hydrocyanic acid, using zinc and hydrochloric acid—



When *amyl alcohol* is used instead of ethyl alcohol with sodium (cf. Baeyer, Ber. **12**, 459) the combination has a much greater reducing power and capacity for adding hydrogen atoms to unsaturated substances.

When used in this way the metal sinks to the bottom of the vessel and may easily crack it. Tafel (Ber. **20**, 250) suggests the

addition of coarse sand, or some similar substance, to prevent contact of the metal with the bottom of the flask and so avoid this danger.

This method has been worked out and applied particularly to the naphthalene derivatives by Bamberger (Ber. **20**, 2,916). The necessary amount of sodium is placed in a flask, and the boiling solution of the substance in amyl alcohol is allowed to flow on to it. The sodium is cut in thin pieces, and a flask with a long neck is selected and is provided with an efficient condenser. The temperature is kept up to the boiling-point of the alcohol till all the sodium has disappeared.

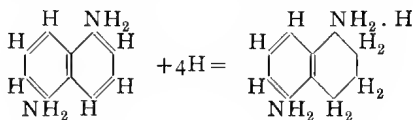
Bamberger noticed at the time of his first experiments that the hydrogenated bases are also formed, but in much smaller quantity, when the sodium is gradually added to the alcoholic solution. When ethyl alcohol was used the yield sank to a minimum, and by far the greater part of the naphthylamine, for example, escaped reduction (see below).

Further details of the method are as follows: For 15 grams of sodium about 150 grams of amyl alcohol are used, and the solution occupies about half an hour. From one and a half to two times as much sodium is taken as the theory requires. When the operation is over the solution is poured into water, and the upper layer is separated and dried with potash. Then the amyl alcohol is distilled off, a vertical tube full of beads being interposed, and the residue is crystallised or fractionated. The yields vary from 40 to 80 per cent. of the theoretical, and in a few cases nearly reach 100 per cent. (Ber. **20**, 3,075).

He has stated in a later paper (Ber. **22**, 944) that the same result may be attained by adding the sodium, in portions of 5 grams, to the boiling solution; that, in fact, this method is preferable to the other since the hydrogen is evolved more gradually and so acts more effectively. It is only when the hydro-base cannot be exposed to a temperature of 130° for any length of time without danger of decomposition that the more rapid method is to be preferred. In either case, care must be taken towards the end of the operation, when the sodium begins to dissolve slowly, to add boiling amyl alcohol to assist the operation.

In the reduction of 1.5 naphthalenediamine (m.p. 189°) he dissolved the base (14 gr.) in boiling amyl alcohol (200 gr.), and added sodium (18–20 gr.) cut in small pieces in portions of five grams at a time. The liquid, which was at first dark-red in colour, became

light brown. The hydrochloride of the 1·5 tetrahydronaphthalenediamine which was formed, being very soluble in water but almost insoluble in amyl alcohol, could be extracted quantitatively by repeated shaking with very dilute hydrochloric acid—



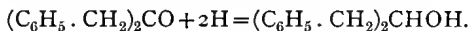
This method has great advantages over the use of hydriodic acid. The operations are carried out in open vessels, and large quantities of the substance can be treated at one time. The results are usually, although not invariably, the same with both agents. For example, the present method brings about the introduction of four atoms of hydrogen into phenanthrene very easily. This result can only be reached otherwise by heating the hydrocarbon with hydriodic acid and phosphorus at 220–240° for six or eight hours. In some cases even, reductions can be effected which are beyond the power of hydriodic acid. Thus retene resists the action of the latter at 100°, while sodium and amyl alcohol introduce four hydrogen atoms. And diphenyl, which had previously been unreducible, and remained intact after heating at 280° with phosphorus and hydriodic acid, was easily converted, to the extent of more than 70 per cent., into a liquid tetrahydro-derivative by the present reducing agent.

Anthracene, on the other hand, takes up only two atoms of hydrogen, while hydriodic acid and phosphorus produce complete hydrogenation. Hydrocarbons containing only one ring are not reducible by sodium and amyl alcohol. The process does not therefore give the most complete hydrogenation, although this might be attained by substituting a product of higher boiling-point, such as secondary octyl alcohol (Ber. **25**, 3,345), which boils at 180°. Still, even this failed in the case of aniline (Ber. **22**, 1,311), and Brühl (Ber. **25**, 1,792) could not reduce camphoric anhydride in solution in boiling naphthalene, using sodium and borneol, an alcohol boiling at 212°, for the purpose.

In *etheral solutions* the sodium is applied by dissolving the substance in five or six times its volume of undried ether and adding the metal to the solution. Or the substance may be dissolved in so much ether, benzene, or other solvent that sodium

will sink in the solution, and this solution may then be floated upon water.

For example, Bogdanowska (Ber. **25**, 1,272) obtained the corresponding secondary alcohol from dibenzyl ketone by dissolving the ketone in ether, pouring this upon a solution of sodium bicarbonate, and throwing in the sodium in small pieces while the flask was kept cold in a stream of water. The operation occupied six or seven days. For each part, by weight, of the ketone at least as much sodium must be taken, and the presence of sufficient sodium bicarbonate to prevent the formation of free caustic soda must be assured. When these conditions are fulfilled the yield reaches 80 per cent. of that theoretically possible—



24. Sodium Amalgam.—The method of using sodium amalgam is similar to that described for sodium, but its action is less energetic than that of the latter.

The amalgam is prepared by gradually adding sodium to mercury in a porcelain mortar. The operation must be conducted under a hood on account of the poisonous mercury vapour which is given off. It usually is made to contain $2\frac{1}{2}$ per cent. of sodium (Taeel, Ber. **22**, 1,870), as the product is then solid and can be pulverised in a mortar and passed through a sieve. Prepared in this way, it should contain no pieces larger than a pea.

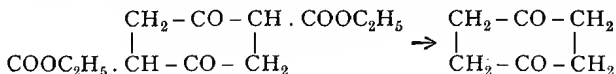
All the experimenters who may be regarded as authorities on the use of sodium amalgam concur in finding that the success with which it may be employed in delicate reactions depends largely on its quality (Ber. **25**, 1,255). Aschan (Ber. **24**, 1,865) uses carefully purified mercury, and brings it in contact with the sodium in a vessel of such a nature that no foreign metal can gain access to it. To avoid the presence of carbon in the amalgam, the sodium should be carefully cleansed from oil. This author suggests that impurities in the mercury may produce electrical currents which bring about the liberation of molecular, and therefore inactive, hydrogen. To Aschan is also due the discovery of the mode of using the amalgam in presence of carbon dioxide, a method which seems to bring out its reducing power most fully. For example, when sodium benzoate is boiled in aqueous solution with sodium amalgam some hydrogen is added indeed; but the action becomes slower and slower as the sodium hydroxide accumulates in the

solution. If the attempt is made to neutralise this from time to time by adding mineral acids, the amalgam dissolves more rapidly, but the hydrogen does not add itself to the benzene ring. But when the alkali is continually removed by carbon dioxide, the addition goes on rapidly to completion. The details of his method are as follows :—

The benzoic acid (50 gr.) is dissolved in a 10 per cent. solution of soda (250 cc.) in a strong flask provided with a vertical tube to condense the vapour. The flask is placed in a large water bath, and the sodium amalgam ($2\frac{1}{2}$ kg.) is added three to four hundred grams at a time. A gentle stream of carbon dioxide is conducted into the solution during the operation. Under these circumstances very little hydrogen escapes as gas. It is necessary occasionally to remove the mercury which accumulates at the bottom of the flask and to add a little water when the sodium bicarbonate begins to crystallise. The reduction occupies from twenty to twenty-five hours, and its termination is marked by the fact that when acid is added to a small sample of the liquid an acid is precipitated which remains fluid in the cold, even after standing for hours. It differs in this respect from benzoic acid, and is in fact tetrahydrobenzoic acid (Ber. **24**, 2,619). It may be remarked in passing that hexahydrobenzoic acid may be prepared from this by adding hydrobromic acid to the remaining double bond, and then replacing the bromine with hydrogen by reduction with sodium amalgam.

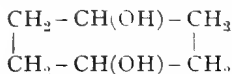
This method of reduction has since been used by Baeyer (Ber. **25**, 1,038) for preparing quinite, the simplest sugar of the inosite group. Maquenne has shown that inosite possesses a closed chain, and is a hexamethylene derivative of the composition $C_6H_{12}O_6$.

By the action of sodium or sodium ethylate on succinic ether succinosuccinic ether is formed. The acid prepared from this substance gives easily diketohexamethylene by loss of two molecules of carbon dioxide—



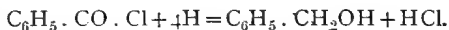
Baeyer added hydrogen to this substance by dissolving the ketone (5 gr.) in sodium bicarbonate, throwing in sodium amalgam (260 gr.), and conducting a rapid stream of carbon dioxide through the

mixture for seven hours. The amalgam was added rather gradually at first. The product, quinite or dioxyhexamethylene—



was similar in appearance and properties to the sugars of the inosite group.

Formerly the method of conducting hydrochloric acid into sodium amalgam used to be employed. Thus Lippmann (*Z. Ch.* **1865**, 700) covered the liquid amalgam with benzoyl chloride, and passed hydrochloric acid into the mixture. The product was benzyl alcohol—



The partial neutralisation of the sodium hydroxide with an acid increases the reducing power and speed of action of sodium amalgam just as it does that of sodium. The way in which the effectiveness of the amalgam varies with the conditions is shown by the number of hydrophthalic acids which Baeyer obtained by its use (*Ann.* **251**, 290). The reduction of lactones in acid solution by Emil Fischer (*Ber.* **23**, 932), in connection with the synthesis of grape sugar, has demonstrated in the clearest way the value of destroying the effect of the free alkali by using some acid, not necessarily carbon dioxide.

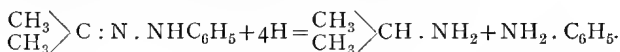
The lactone, or syrup containing the lactone, is dissolved in ten parts of water in a bottle. The liquid is slightly acidified with sulphuric acid, placed in a freezing mixture until ice begins to form, and then a small amount of $2\frac{1}{2}$ per cent. sodium amalgam is added. When the whole is violently shaken the amalgam is quickly exhausted without evolution of hydrogen gas. This process is repeated, with occasional cooling and frequent addition of sulphuric acid to preserve the acid reaction of the liquid, until finally towards the end of the operation hydrogen is given off. It is best to determine the quantity of amalgam which is required by titrating a small sample of the liquid, say 2 cc., with Fehling's solution from time to time. When the reduction of Fehling's solution reaches a maximum the action is complete. Pure lactones require ten to fifteen times their weight of amalgam of the above strength.

Weidel (*M. f. Ch.* **11**, 510) reduced nicotinic acid (40 gr.) in alkaline solution by dissolving it in 25 per cent. caustic potash. To the boiling solution he added gradually 4 per cent. sodium

amalgam until the evolution of ammonia ceased. The operation occupied from three to four hours.

The amalgam is used also in alcoholic, ethereal, and acetic acid solutions. For example, Claus (Ann. **137**, 92) dissolved benzaldehyde in five or six times its weight of moist ether, and added excess of semi-solid amalgam. An energetic action took place, so that cooling was necessary to keep the ether from boiling. The products were freer from coloured by-products the lower the temperature was kept.

Tafel (Ber. **22**, 1,855) has devised a very convenient way of preparing amines by the reduction of hydrazones. Phenylhydrazine reacts quantitatively with aldehydes and ketones, and the products give two amines on reduction. For example, acetone phenylhydrazone gives isopropylamine and aniline—



The operation is carried out as follows: The hydrazones are dissolved or suspended in from ten to twenty times their weight of alcohol, and to this solution, which is continually cooled and shaken, portions of acetic acid (25 cc.) and $2\frac{1}{2}$ per cent. amalgam (250 gr.) are added from time to time. The temperature must be kept constant within two or three degrees, and care must be taken that excess of acetic acid is always present. About twice the amount of amalgam which is theoretically necessary must be used. About two hours will be required for working up 3,500 grams of the amalgam. Towards the end of the action sodium acetate is deposited. The liquid is finally rendered alkaline with caustic soda and distilled. Bases of high boiling-point are separated from aniline by Tafel by carefully neutralising the aqueous distillate with sulphuric or hydrochloric acid and concentrating on the water bath. Extraction with ether then removes the aniline.¹

25. Sulphurous Acid.—Sulphurous acid exercises a reducing action towards very few substances, and is chiefly used for the conversion of quinones into quinols. The gas is conducted through an aqueous solution of the quinone. In the case of quinone itself the liquid first becomes brown, owing to the formation of quinhydrone, and then loses its colour again when this is converted into quinol (cf. Chap. XVIII. §45).

¹ Cf. Miller's method, § 29.

Neumann (Ber. **20**, 1,584) states that sulphur dioxide can be generated in a Kipp's apparatus by charging it with common concentrated sulphuric acid and a mixture of calcium sulphite (3 parts) and gypsum (1 part) made up into little cubes. Half a kilogram of this material will give a continuous stream of the gas for thirty hours.

Claus and Berkefeld (J. pr. Ch. **151**, 585) found that the reduction of 4.5 dichloroorthoxylo 3.6 quinone presented extraordinary difficulties. Even when an ethereal solution was shaken with stannous chloride and hydrochloric acid no reduction took place. The substance had to be heated at 100° with concentrated aqueous sulphurous acid in a sealed tube.

Sodium hyposulphite, NaHSO_3 , which might be expected to be a valuable reducing agent, does not seem to have received any application in this direction. Experiments of the author's, in one particular case, where a favourable result might have been anticipated, showed that no reduction had been effected.

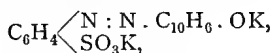
26. Tin.—This metal can be used either in acid or alkaline solution.

The metal is applied either granulated or in the form of foil (Ber. **23**, 1,626). Treadwell (Ber. **25**, 2,381) states that tin is best granulated by melting at as low a temperature as possible, and pouring through a sieve made of sheet iron containing a few holes, which is held just above the surface of a vessel of cold water. The metal obtained in this way consists of solid pear-shaped uniform grains half the size of a pea. The acid employed is usually hydrochloric, occasionally hydrobromic, because, after the tin has been taken out with hydrogen sulphide, these acids can be removed by evaporation on the water bath. Under these conditions therefore the substances used for reduction can easily be separated from the products. The process originated with Beilstein (Ann. **130**, 243).

Reductions by this method sometimes occupy much time, especially when conducted in the cold. Lossen (Ann. Suppl. **6**, 221), for example, allowed nitric ether to remain in contact with the mixture for fourteen days in order to obtain the maximum yield of hydroxylamine. On the other hand the action may be so violent that the substance to be reduced must be added in small portions, or drop by drop, to the reducing mixture, which is often maintained at the boiling temperature during the action (Ber. **12**, 2,039). Strong hydrochloric acid is generally employed.

Even when the acid liquid is very greatly diluted, the precipitation of the tin by hydrogen sulphide may be incomplete. Since the sulphide formed in the cold is with difficulty retained by a filter, it is advisable, whenever possible, to pass the hydrogen sulphide into the liquid in the heat. To drive off the free hydrochloric acid the liquid must be evaporated. The naked flame can be used at first for this purpose. When hydrogen sulphide is passed through the liquid for the second time a further precipitation of sulphide takes place. The filtrate, after further evaporation, must be tested for tin again, and this process repeated until all the metal is finally thrown down.

During the concentration the hydrochloride of the base, being usually insoluble in strong hydrochloric acid, begins to crystallise out. This fact may even be taken advantage of for the purpose of isolating the base without first precipitating the tin. This method is exemplified in Seidel's process (Ber. **25**, 423 and 976) for making amidonaphthol hydrochloride. One kilogram of the potassium salt of benzeneazonaphtholsulphonic acid—



which is sold as a dye under the name of "Orange I.," is mixed with five litres of water and brought into solution by passing steam through the mixture. The boiling liquid is poured into five litres of warm concentrated hydrochloric acid of sp. gr. 1.19 containing the calculated amount of stannous chloride. Almost the whole of the amidonaphthol hydrochloride is at once precipitated, and is found to be free from tin and from sulphanilic acid. The latter forms a soluble salt with the hydrochloric acid. As soon as the liquid has cooled to 40–50° it is filtered, and the crystals are washed with dilute hydrochloric acid. The yield is 360 grams.

A somewhat different method of isolating the product of the reduction was used by Hübner (Ann. **208**, 304). Benzorthonitrilide (10 gr. = 1 mol.) was mixed with the necessary amount of finely granular tin (3 atoms), and the mixture was made into a thin paste with strong crude hydrochloric acid. This was gently warmed in a flask until the anilide had gone completely into solution. Since under these circumstances stannous chloride and hydrochloric acid give off some hydrogen, a part of the tin remains undissolved. The solution is poured off and evaporated to dryness, and the residue is stirred up with a little saturated ammonia water, and

warmed with yellow ammonium sulphide to dissolve the sulphide of tin. At first only a little ammonium sulphide is added, and the amount is gradually increased until the solid residue does not seem to decrease in quantity. This substance, the product of the reduction, is then collected on a filter, and thoroughly washed with water. It is needless to add that this process can only be used with bases which are insoluble in water.

Insoluble bases can also be isolated by rendering the solution alkaline with caustic soda, which precipitates the base. The latter can be purified by recrystallisation (Ber. **15**, 1,920, and **20**, 1,878). In this case the prior removal of the tin and hydrochloric acid is unnecessary, as the hydroxide, which is at first precipitated, redissolves in excess of caustic soda, and the acid is of course neutralised. When the base is volatile with steam it is best to use this method for removing it from the alkaline mixture.

Many solutions containing reduced substances have the disagreeable property of becoming dark in colour during evaporation, after the last traces of tin have been removed with hydrogen sulphide.

This is usually attributable to oxidation by air, and may be prevented by conducting the evaporation in a flask provided with a Bunsen valve. Or a suitable reducing agent may be introduced by passing hydrogen sulphide through the solution, or adding sulphurous acid or sodium hyposulphite to it. Even a drop of a stannous chloride solution may be used (Ber. **20**, 1,148).

If the base is likely to suffer decomposition by being evaporated with hydrochloric acid after the removal of the tin, it may be set free by adding sodium carbonate, and removed by filtering or extraction (Ber. **25**, 860).

Another method consists in neutralising the acid by shaking with lead hydroxide (cf. Chap. XVIII. § 32) or moist silver oxide after the tin has been removed. If any of the metal passes into solution it can be precipitated with hydrogen sulphide from the filtrate. It may be remarked here that silver chloride is soluble in very strong hydrochloric acid.

Hlasiwetz and Habermann (Ann. **169**, 155) have found that cuprous oxide may be used for the removal of the greater part of the hydrochloric acid in such solutions. They warmed the acid solution to 50° in a flask, and added a paste of cuprous oxide, shaking after each addition, until the red colour of the foam showed that an excess of the oxide was present. The liquid standing over the precipitate was seen to be blue owing to the presence of copper,

and was consequently by no means free from chlorine. The liquid was filtered, and the copper precipitated with hydrogen sulphide. The filtrate was then concentrated, and the remainder of the hydrochloric acid was removed with silver oxide.

The cuprous oxide may be most conveniently prepared by Mitscherlich's method (J. pr. Ch. **19**, 450). Caustic soda is added to a solution containing equal parts of cupric sulphate and grape sugar until the cupric hydroxide at first precipitated is redissolved. When this solution is warmed, the cuprous oxide is thrown down as a powder, which is free from hydroxide, and is not changed by exposure to the air.

If the hydrochloride is stable while the base itself is unstable the method applied by Pukall (Ber. **20**, 1, 148) to *o*-amidodiethylresorcinol may be used. This base was extremely unstable when moist. He therefore saturated the solution of the pure hydrochloride with hydrogen sulphide, and precipitated the base with lime water or sodium carbonate. The crystalline scales which appeared were washed with water containing the same gas, and dried in a place free from draughts. Even this last process was better carried out in an indifferent atmosphere.

It has long been known that when nitro-bodies are treated with zinc or tin and hydrochloric acid, chloroamido-compounds are sometimes formed. Their formation can be entirely excluded by reducing with tin and acetic acid. For example, Fittig (Ber. **8**, 15) states that when he used the former way he obtained chlorobromaniline along with bromaniline from *p*-bromonitrobenzene. Kock (Ber. **20**, 1, 569) reduced nitrobenzene (70 gr.) with zinc and hydrochloric acid, and found that aniline (29 gr.) and pure *p*-chloraniline (17.5 gr.) were formed.

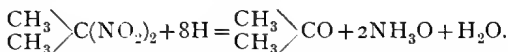
V. Miller and Rohde (Ber. **23**, 1, 891) reduced *p*-nitrohydrocinnamic acid (25 gr.) by treating it with tin (45 gr.) and hydrobromic acid of sp. gr. 1.49 (165 gr.) at a low temperature.

Tin and hydrochloric acid are also used for reduction in alcoholic solution. For example, Friedländer and Weinberg (Ber. **15**, 1, 422) added these substances to a hot alcoholic solution of *o*-nitrocinnamic ether until, when the violence of the action had somewhat abated, no turbidity was produced by adding water. The tin was removed with hydrogen sulphide, and the amido-ester precipitated in yellow needles by addition of sodium acetate (Chap. II. § 2). When ten or twenty grams of the substance were used the action took place quantitatively.

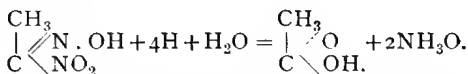
The use of ethereal solutions also has been introduced by Friedländer and Mahly (Ber. **16**, 852). They found the problem of reducing dinitrocinnamic ether presented great difficulties on account of the instability of that compound. Alkaline reducing agents are necessarily unsuitable. And on the other hand, when acids are present, a part of the nitrogen is lost in the form of ammonia, and easily soluble oxy-acids are formed. To diminish the violence of the action therefore the ester was dissolved in small portions, each in ten or twenty grams of ether, concentrated hydrochloric acid and granulated tin were added, and the mixtures were allowed to remain in the cold for twelve hours. When the action was over the yellow solutions were diluted with water, and the ether and tin were removed. Then the acid was neutralised with soda and the liquids concentrated. Finally, they were evaporated to dryness with hydrochloric acid, and the diamidohydrocinnamic acid was extracted from the residue with alcohol.

As a general rule, when substances are reduced with tin and hydrochloric acid each nitro-group is replaced by an amido-group, but this seems only to hold so long as not more than one nitro-group is attached to the same carbon atom.

For example, Victor Meyer and Locher (Ber. **8**, 215) have found that when dinitropropane is treated with tin and hydrochloric acid, acetone and hydroxylamine are formed instead of the expected product—

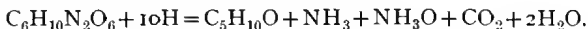


Ethyl nitrolic acid gives hydroxylamine and acetic acid under the same conditions—



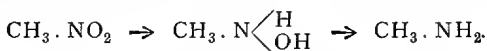
With sodium amalgam the products are quite different.

Kachler (Ann. **191**, 164) reduced dinitroheptylic acid with tin and hydrochloric acid, obtaining methylisopropylketone, ammonia, hydroxylamine, and carbon dioxide—



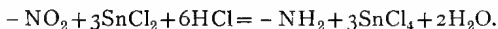
Hoffmann and Meyer (Ber. **24**, 3,528) state that very extraordinary intermediate products, which are extremely hard to isolate, may be formed in these reductions. Thus nitromethane

gives methylhydroxylamine, which subsequently passes over into methylamine—



27. Tin Bichloride.—Many reductions can be carried out more easily with an acid solution of stannous chloride than with tin and hydrochloric acid. This was first observed by Spiegelberg (Ber. 11, 35). He added the nitro-compound which was to be reduced to a clear solution of stannous chloride, containing about 150 grams of tin per litre dissolved in excess of acid. The action usually began without the aid of external heating when the ingredients were mixed, and, if large quantities were worked up at one time, often became so violent as to lead to boiling and frothing over of the mixture.

The facility with which this action took place led Limpricht to make experiments in regard to its suitability as a method for the quantitative estimation of the NO_2 groups in organic compounds. The action is represented by the equation—



It was found that as a matter of fact an accurate estimate of the proportion of NO_2 contained in the compound could be made by titrating the excess of stannous chloride which remained after the reduction. When the nitro-body is volatile, the operation is carried out in a sealed tube at the temperature of the water bath.

Experience has shown that a proportion of 40 grams of bichloride to 100 cubic centimetres of acid of sp. gr. 1.17 gives the best reducing liquid for most purposes, although in special cases variations from this may be advisable.

A process for reducing perchloromercaptan, CCl_3SCl , to thiophosgene, CSCl_2 , which is described in a patent applied for by Kern, will illustrate the use of this method. The patent was not granted for some unknown reason. Crystallised stannous chloride (27 parts) is dissolved in hydrochloric acid (10 parts) and water (7 parts), and perchloromercaptan (20 parts) are added. The mixture is digested for twelve hours at $30\text{--}35^\circ$, the air being excluded, and the whole being vigorously stirred during the process. Finally, the thiophosgene is separated mechanically or distilled off.

Any one who has tried Rathke's method (Ann. 167, 204) for reducing perchloromercaptan to thiophosgene with finely divided

silver will recognise the advance which has been made in the art of reduction during the last eighteen years. In Rathke's time the other known methods were even less effective in this particular case.

It is often desirable to add some metallic tin to the acid solution of stannous chloride.

Stannous chloride is one of the few reducing agents with whose help anything can be made of the reduction of bases containing nitrobenzyl groups. For example Lellmann and Mayer (Ber. **25**, 3,584) made many vain attempts to prepare *o*-diamidodibenzylaniline. Finally, they succeeded by placing finely pulverised dinitrodibenzylaniline, $C_6H_5N(CH_2 \cdot C_6H_4 \cdot NO_2)_2$ (3 gr.), and stannous chloride (15 gr.) in a small flask, and adding glacial acetic acid and an equal volume of concentrated hydrochloric acid (50 gr.). The mixture was cooled during the whole process and repeatedly shaken. The cooling prevents the action becoming too rapid, and the operation occupies several hours. It is complete when no small yellow particles of the nitro-compound are visible mingled with the tin double salt which forms. The base is isolated by treating the double salt with excess of ammonium sulphide, and crystallising the residue from benzene (cf. p. 314).

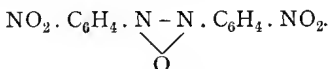
The following process was used by Brunner and Witt (Ber. **20**, 1,025). Orthodinitrodiamidodiphenyl was mixed with the requisite amount of the bichloride, hydrochloric acid was added, and the mixture was warmed on the water bath until no precipitate was produced on adding water to a sample. Tin was then added, and the warming was continued until the stannic chloride which had been formed was itself reduced. The liquid was then greatly diluted and freed from tin with hydrogen sulphide. The product was the hydrochloride of tetramidodiphenyl.

Many observers recommend the preparation of the stannous chloride just before use on account of the questionable quality of the commercial article. The solution is made by dissolving 200 grams of tin in a litre of concentrated hydrochloric acid, and adding a few cubic centimetres of concentrated sulphuric acid. Grandmougin and Michel (Ber. **25**, 981) suggest that it is well not to add all the acid at once. They add first one third of the quantity to the tin, and further portions when the slower rate at which the metal begins to be dissolved seems to demand it. The final addition of a few drops of platinum tetrachloride or cupric chloride is advised.

Stannous chloride is soluble also in alcohol, and can consequently be dissolved in alcoholic hydrochloric acid. Victor Meyer (Ann. **264**, 131) states that the alcoholic solution of the salt is often an excellent reducing agent. It acts smoothly, and frequently succeeds

where other reducing agents fail entirely or give the products in such a condition that they cannot be isolated.

Willgerodt (Ber. **25**, 608) used this method in reducing *m*-dinitrobenzene to *s-m*-dinitrazoxybenzene—



Claus (J. pr. Ch. **151**, 565) found it necessary to boil dinitrodi-bromocymene for twelve hours with the alcoholic solution to complete its reduction. Schulhöfer and Meyer (Ann. **264**, 131) found in nitroindazol carboxylic acid a substance whose nitro-group was proof against every reducing agent even including the present. By long warming on the water bath it seemed only to take up hydrogen by addition.

With the solution of stannous chloride, as with ammonium sulphide, it is in one's power to reduce by successive steps the nitro-groups of a substance containing more than one. Thus Lauterbach (Ber. **14**, 2,029) mentions that in reducing dinitronaphtholsulphonic acid with the solution of bichloride in hydrochloric acid a nitroamido-acid is formed intermediately, although he made no attempt to isolate it. Nietzki (Ber. **16**, 2,094), treating the potassium salt of nitranilic acid in aqueous solution, obtained a substance to which he assigned the constitution of a nitroamido-tetroxybenzene, $\text{C}_6(\text{OH})_4\text{NH}_2\text{NO}_2$. A method for the step-by-step replacement of nitro- by amido-groups in aromatic bodies, which is of quite general applicability, in which the use of the alcoholic solution is essential, has been devised by Anschütz (Ber. **19**, 2,161)

For example, he prepares nitraniline easily by dissolving *m*-dinitrobenzene in alcohol, and allowing the calculated amount of stannous chloride dissolved in alcohol saturated with hydrochloric acid to flow in drop by drop while the mixture is kept cool and constantly shaken. By the same process he obtains *o*-amido-*p*-nitrotoluene from *o-p*-dinitrotoluene. The *o*-nitro-*p*-amidotoluene which is the sole product when alcoholic ammonium sulphide is used in the cold, could not be traced in the product formed by stannous chloride. The interesting fact is brought out by this that the nitro-group selected by stannous chloride for reduction is the very one which is spared by ammonium sulphide.

Claus (Ber. **20**, 1,379) discovered this property of the alcoholic solution almost simultaneously with Anschütz. He dissolved, for example, dinitrochlorobenzene in absolute alcohol, added concentrated hydrochloric acid, and allowed this mixture to flow gradually into the amount of stannous chloride necessary for the reduction of one nitro-group.

A mixture of one part of glacial acetic acid and one part of concentrated stannous chloride solution is also used for reduction.

It may be well here to recall the fact that in the decomposition of complex bodies like the protein substances (Ann. **169**, 151), with hydrochloric or other non-oxidising acids, the addition of stannous chloride supplies the best means of preventing the formation of coloured secondary products. In fact, all decompositions of this kind seem to proceed more smoothly and sharply in its presence.

If some other metal being present in the solution would have less disturbing effect than tin, or if it is desired to recover the tin on account of its value, clippings of zinc may be added to the liquid. This causes the precipitation of the metal in a very finely divided condition, which renders it particularly valuable for later use in other reductions (Ann. **247**, 291).

On account of the tendency of stannous chloride to pass over into stannic chloride, and consequently to act as a reducing agent, it is impossible to convert the amides into diazo-bodies directly in the solutions in which they occur. On the other hand, zinc chloride interferes in no way with the accomplishment of this additional step. So that when the latter metal is used there is no need of removing it from solution before working up the product further.

The *alkaline solution of tin* is also in frequent use as a reducing agent. Böttger and Petersen (J. pr. Ch. **112**, 327) were the first to recommend the use of this substance. They prepared the solution by adding finely pulverised stannous chloride to rather strong caustic soda or caustic potash until a precipitate of stannous hydroxide began to form. The mixture was thoroughly stirred during the process, and finally filtered to obtain a clear solution. To reduce dinitroanthraquinone they boiled it with this solution for a considerable time.

This method has acquired great importance since Witt (Ber. **18**, 2,912) founded on it a process for the preparation of azo-bodies. In Griess' methods we have very convenient ways of preparing quantitatively azo-compounds containing hydroxyl- and amido-groups. But for making other azo-compounds we have almost entirely to rely on the reduction of the corresponding nitro-bodies. Zinin's method, in which alcoholic alkalis are used, is only successful in isolated cases. Klinger's method, by reduction with sodium, can

only be applied to such nitro-compounds as are soluble in alcohol. Sodium amalgam would be more applicable if the difficulty of recognising when the action is completed were not so great. Zinc dust is used with caustic potash and with a solution of calcium chloride, but difficulties are met with in the separation of the azo-body from the pasty product of the action. This can only be accomplished by repeated extraction with alcohol. The method of Weselsky, which consists in fusing nitrophenols with potassium hydroxide, is only applicable to a limited number of substances.

In view of the limitations of these methods therefore, Witt introduced the solution of stannous hydroxide (Prometheus, **2**, 640) as being a more suitable reducing agent. The calculated amount of stannous chloride is dissolved in water and added to excess of cold caustic potash. The clear solution is then allowed to act upon the nitro-body at the temperature of the water bath. If the body is liquid or easily melted it suffices to shake it with the prepared solution. If the substance is soluble in alcohol the solution in this solvent may be added to the alkaline solution. In this case the reduction is energetic and is soon complete. Finally when nitro-sulphonic acids are in question an aqueous solution of a salt may be added to the reducing agent.

In the last case, that of nitrosulphonic acids, it is far preferable to use the potassium salts rather than the sodium salts, and to work with a solution of stannous hydroxide in caustic potash, as the potassium salts of the azosulphonic acids formed are usually less soluble and crystallise better than the sodium salts.

As a general rule the azo-body crystallises out without further trouble when the solution cools. When this does not occur the tin is precipitated with carbon dioxide, and the solution is concentrated until crystallisation begins. In some cases it may be necessary, however, to separate the azo-body from potassium carbonate with dilute alcohol.

Friedländer (Ber. **22**, 587) finds that the reduction of diazobodies to hydrocarbons is best accomplished by the alkaline solution of stannous hydroxide. The method of Griess by boiling with alcohol often fails, as in the case of *p*-diazoxylene. Fischer's conversion into the hydrazine and oxidation of the latter with ferric chloride (Ber. **23**, 2,672) usually gives better yields, but is too laborious.

Friedländer's method, which performs the reduction in the absence of alcohol, avoids these difficulties. He takes advantage

of the fact that most diazo-derivatives are soluble without decomposition in excess of cold caustic soda. This alkaline solution is usually as stable as the acid solution. But when an alkaline reducing agent is added a vigorous evolution of nitrogen begins even in the cold, and the nitrogen is replaced by hydrogen.

The application of this method to aniline will serve as an example. The aniline is first converted into diazobenzene chloride, and the faintly acid solution, which should not be too dilute (1 : 10, or 1 : 20), is poured into cold caustic soda containing pieces of ice. When a solution of stannous chloride in caustic soda is added to the clear alkaline solution, nitrogen gas is given off rapidly even at the ordinary temperature, and when the action is at an end a layer of benzene is found floating on the surface. Similarly *α*-naphthylamine gives naphthalene and sulphanilic acid, benzenesulphonic acid. This method is specially useful where the product of the reduction is insoluble in caustic soda, as is the case with hydrocarbons.

28. Zinc.—This metal is not so frequently used as tin. Like the latter it can be used in alkaline or acid solution, and can even be employed in neutral liquids in addition.

Hydrogen is given off when zinc and iron are brought in contact with ammonium and amine salts in water even at the ordinary temperature, and better still at or above 40°. Lorin (Ann. **139**, 374) found that when zinc and iron acted on an aqueous solution of ammonium sulphate at the temperature of the room, acetone, which had been added to the solution, was reduced to isopropyl alcohol.

Leykauf states (J. pr. Ch. **19**, 124) that when sheet zinc is introduced into a solution of sulphate of copper in three times its weight of water a considerable amount of hydrogen is evolved.

Liebermann and Scholz (Ber. **25**, 950) succeeded in replacing the bromine atom in the addition product of phenylpropionic acid and hydrobromic acid by hydrogen, without at the same time saturating the remaining double bond with the same element. They accomplished this by boiling the bromocinnamic acid with twice its weight of zinc filings—not zinc dust—and ten times its weight of absolute alcohol for three or four hours in a flask provided with a condenser.

Usually, however, the metal is used as a reducing agent in *alkaline solutions*. In order to give as large a surface as possible

it is melted in the flame of a blast lamp and allowed to fall in single drops on clay plates. The zinc foil so obtained can afterwards be cut in pieces if necessary. When the action is over the zinc can be precipitated with carbon dioxide. Both aqueous and alcoholic caustic potash are used as solvents. Zagoumenny (Ann. **184**, 175) finds that the latter works particularly well in the reduction of aromatic ketones to alcohols. Thus benzophenone gives diphenylcarbinol when treated by this method, while with zinc and acetic acid it gives benzpinacone.

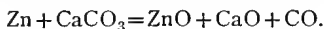
Zinc is also used in *acid solution*, generally alcoholic. Years ago Girard (Ann. **100**, 306) converted carbon disulphide into trimethylene sulphide, $(CH_2S)_3$, by this method. The process now generally used is to place zinc in the solution to be reduced and add hydrochloric or acetic acid from time to time. For example, Bischoff (Ann. **251**, 305) dissolved *o*-nitrobenzoylmalonic ether (5 gr.) in absolute alcohol (50 gr.), added pure zinc clippings (14.7 gr.) to the cold solution, surrounded the whole with ice, and passed a stream of dry hydrochloric acid gas through the mixture.

The use of acetic acid has the advantage over that of mineral acids that the metal can afterwards be precipitated with a current of hydrogen sulphide.

Perkin (Ber. **16**, 1,031) used a copper-zinc couple and acetic acid for reductions. Gladstone and Tribe (J. Ch. Soc. **45**, 154) applied the same method to the preparation of methane from methyl iodide, and obtained 99 per cent. of the calculated quantity. They poured a two per cent. solution of cupric sulphate over granulated zinc, leaving the substances in contact till the liquid became decolourised, and repeated the process with the same zinc three or four times. The zinc being plated with copper was well washed and moistened with alcohol. It was then placed in a 600 cc. flask provided with a vertical tube 36 cm. long and 3 cm. in diameter to act as a condenser. The condensing tube, which was partially drawn out at the bottom, was connected with the flask by a stopper with two openings. The stem of a separating funnel containing alcohol and methyl iodide and provided with a stopcock passed through the second opening. Another similar stopper closed the upper end of the tube, and was provided with holes for another separating funnel containing alcohol to moisten the zinc-copper and a tube to conduct off the gas. Forty-five grams of methyl iodide gave seven litres of methane in less than an hour and a half. Somewhat later Weigh recommended that the escaping gas

should be further purified by being led through a series of tubes containing the same zinc-copper couple moistened with alcohol.

29. Zinc Dust.—In this form the metal has extremely powerful reducing qualities. It even decomposes chalk quantitatively when a mixture of the substances is heated in a combustion tube (Ber. **19**, 1,141)—

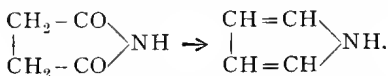


It is obtained during the manufacture of zinc, and collects in the iron receivers into which the metal is distilled from tubes or retorts. The first part of the distillate consists of zinc dust, which is a mixture containing 10 to 20 per cent. of zinc oxide, and often some cadmium.

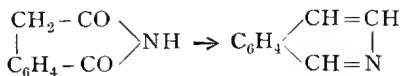
We owe to Baeyer the introduction of this valuable reducing agent. It is particularly applicable to the reduction of aromatic substances, and gives the corresponding hydrocarbons as the result of its action. By its use Gräbe and Liebermann (Ber. **1**, 49) reduced alizarin to anthracene. This led them to achieve the artificial preparation of alizarin from the hydrocarbon anthracene, which occurs in large quantities in coal tar.

In distilling with zinc dust, a large excess of the metal is always used. The operation is best carried out by heating the mixture in hard glass tubes in a combustion furnace, while a stream of hydrogen or carbon dioxide is conducted through the apparatus. If the action is too energetic, dry sand may be mixed with the substance.

Its value may be illustrated by mention of its use in converting nitrogen compounds of substances with a simple carbon chain into compounds containing rings. Thus Bernthsen (Ber. **13**, 1,047) distilled the imide of succinic acid with zinc dust, and obtained pyrrol—



Following this up, Leblanc (Ber. **21**, 2,299) distilled homophthalimide, which differs from the above imide in having a C_6H_4 in place of the CH_2 group, with the same reagent, and succeeded in synthesising isoquinoline—



When simply *boiled with water*, zinc dust exhibits great reducing power. Miller (Ber. **13**, 269) therefore recommends its use in this way in cases where it acts as effectively without acids as in their presence, since under those circumstances it forms no zinc salts whose presence might interfere with the isolation of the products of the reduction. He uses this method particularly for the decomposition of azo-dyes. These bodies split at the double linkage between the nitrogen atoms, and take up hydrogen, forming amido-compounds. For example, chrysoidine, $C_6H_5 \cdot N : N \cdot C_6H_3(NH_2)_2$, breaks up into aniline and triamidobenzene.¹

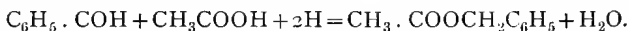
Usually, however, *acids are added*, and as a general rule aqueous or alcoholic hydrochloric acid is employed. Reductions by this method ordinarily take a good deal of time. For example, Schlieper (Ann. **239**, 237) boiled an alcoholic solution of α -naphthindole, adding zinc dust and hydrochloric acid from time to time, until a splinter of pine was no longer coloured bluish violet when dipped in the liquid. The change into α -hydronaphthindole was easy to trace, but the conversion of 5 grams occupied 12–15 hours.

Krafft's work (Ber. **16**, 1,715) exhibits fully the value of using zinc dust for reductions in presence of acetic acid. The advantages of this easily prepared reducing mixture are that it generally retains the organic substance in solution, it is not rapidly used up even when heated for a considerable period, and the chief product of the action can usually be separated from it without much loss of material or time. When the glacial acid is used the metal is but slowly attacked even in the heat, unless very easily reducible substances are present, and the zinc salt collects in compact crusts, so that the action of the acid is not interfered with up to the very end of the operation. Thus the soluble product can finally be obtained almost instantly by pouring off the acetic acid solution and adding water to it. If insoluble in the latter, the new body is at once precipitated. When glass vessels are used, very energetic digestion is out of the question, and under these circumstances a part of the metal will be protected by the deposition of the zinc acetate upon it. This difficulty can be avoided, however, by adding the dust at intervals of two or three days. In this way a sufficient amount of active surface can be maintained without the use of an excessive quantity of the metal altogether. This method was used

¹ Cf. Tafel's method, end of § 25.

by Krafft for the reduction of aldehydes to alcohols. The latter were isolated in the form of esters of acetic acid.

The difficulties which Tiemann encountered (Ber. **19**, 354), in attempting to obtain a well-characterised alcohol glucoside from glucoferulic aldehyde by the action of sodium amalgam and water, led him to investigate the use of zinc dust and glacial acetic acid in reducing aldehydes to alcohols. For example, he boiled benzaldehyde with this reducing mixture for twelve hours in a flask connected with a reflux condenser. The supernatant liquid was then poured off the excess of zinc dust and the precipitate of zinc acetate into a vessel of water. The product was then neutralised with soda or chalk and extracted with ether. The substance formed was found to be benzyl acetate so that the alcohol had at once passed over into the ester—



In the case of oxybenzaldehyde (Ber. **24**, 3,170), however, the same process led to the formation of complicated products.

Dilute acetic acid is also very useful, especially when the substance to be reduced is insoluble in glacial acetic acid. For example, Fischer and Tafel (Ber. **22**, 99) found that α -acrosone was completely reduced when heated on the water bath for an hour in dilute aqueous solution with zinc dust and acetic acid. They filtered the resulting liquid, precipitated the zinc with hydrogen sulphide, and evaporated the filtrate *in vacuo* on the water bath. When the residue was taken up with absolute alcohol, the solution filtered and ether added to the filtrate, α -acrose was thrown down. This substance, the first sugar to be prepared synthetically, ferments with yeast like ordinary sugar, but is optically inactive.

Fischer and Hepp (Ber. **21**, 680) treated anilidonaphthoquinoneanil (15 gr.) with zinc dust (70 gr.) and a mixture of glacial acetic acid (200 gr.) and sulphuric acid (50 gr.) diluted with water (50 cc.). The products were aniline and naphthalene.

V. Pechmann found (Ber. **25**, 3,188) that when formazyl hydride was boiled with acetic anhydride and zinc dust, hydrogen was added and an acetyl derivative was formed.

Zinc dust is used in *alkaline solutions* also as a reducing agent. The substance may be boiled with aqueous or alcoholic ammonia and zinc dust in a flask connected with a condenser. The alcoholic ammonia is made from sixty per cent. alcohol.

For example, Wohman (Ann. **259**, 283) dissolved a diazo-compound in ten or twenty per cent. ammonia, and added zinc dust in small portions. The solution became slightly warm during the process. As soon as no more heat was developed, the mixture was

filtered with the help of a pump, and the hydrazine derivative was extracted from the filtrate with ether.

Elbs (J. pr. Ch. **149**, 15) found the following to be the only suitable method for reducing *m*-dimethylantraquinone. The substance, in quantities of five grams, was finely pulverised and mixed intimately with zinc dust (30 gr.). Concentrated aqueous ammonia (200 cc.) and a solution of basic carbonate of copper in ammonia (5 cc.) were then poured on to it. When this mixture was shaken up it became warm. The whole was boiled for six hours, and during this operation portions of a few cubic centimetres of the same solution of carbonate of copper were added at short intervals. When the whole had cooled it was filtered, the filtrate was evaporated to dryness, and the residue was extracted with alcohol. The quantity of the hydrocarbon which was so obtained was about 20–25 per cent. of the original substance.

When the boiling is prolonged, fresh ammonia must be added from time to time.

The result is not always perfectly satisfactory. Thus Lautebach (Ber. **14**, 2,030) dissolved dinitronaphtholsulphonic acid in a litre and a half of water, added zinc dust, and, after a short interval, ammonia. He obtained a blood-red solution, which deposited crystals, having the composition $C_{20}H_{18}N_3O_{12}S_2$ instead of the expected reduction product.

Caustic soda and caustic potash are frequently used instead of ammonia.

Messinger (Ber. **18**, 1,636) used this method in reducing mono- and di-iodothioxene to thioxene. At first he caused sodium to act on the alcoholic solution, but this process was found to have many disadvantages. For example, not more than twenty grams of the substance could be treated at one time, the action was besides very slow, and the mixture had to be shaken continuously. Then, too, a good deal of the thioxene was carried off by the great amount of hydrogen evolved during the continuance of the process, and even at the end the reduction was incomplete, and a rather tedious separation of the thioxene from the iodo-derivatives was necessary.

All of these disappeared when zinc dust and alcoholic caustic soda were used. The caustic soda (100 gr.) was dissolved in alcohol (400 gr.), and the iodothioxenes (100 gr.) were added to the cold solution. Then zinc dust (150 gr.) was put into the mixture, and the whole was warmed on the water bath in a flask attached to a condenser for an hour. At the end of this time the reduction was

complete, and the thioxene and alcohol were driven over in a current of steam.

Barsilowsky (Ann. **207**, 115) found that *m*-azotoluene, $\text{CH}_3 \cdot \text{C}_6\text{H}_4 \cdot \text{N} : \text{N} \cdot \text{C}_6\text{H}_4 \cdot \text{CH}_3$, could easily be made from *m*-nitrotoluene by gently warming the latter with zinc dust and alcoholic potash and then extracting with ether.

Ladenburg (Ann. **217**, 11) recommends the use of a small amount of iron filings with the zinc dust. Probably the addition of a little of the ammoniacal copper solution, which gives rise to the formation of the copper-zinc couple, is equally effective.

He found that chlorotropic acid could not be reduced by sodium amalgam. He therefore dissolved the acid gradually in ten times its weight of concentrated caustic potash, and added zinc dust and some iron filings to the solution. The reducing agent was allowed to act for two days at the ordinary temperature, and small quantities of the metals were added from time to time so that a slow evolution of hydrogen gas was perceptible during the whole operation. Finally, the mixture was diluted with water and filtered. The filtrate was acidified with hydrochloric acid, and the zinc precipitated with carbonate of soda. The final filtrate was acidified again, and the tropic acid was extracted with ether.

Bamberger and Berl  (Ber. **24**, 3,208) attempted in vain to reduce carvacrol by dissolving it in fused potassium hydroxide at 180–220° and adding zinc dust.

We owe to Dechend (Ger. Pat. 43,230) the method of reducing nitro-bodies by means of zinc dust, with or without iron filings, and an aqueous solution of a salt.

For example, he heated nitrobenzene (100 gr.) to 130°, and added to it an aqueous solution of calcium chloride boiling at 103° (100 gr.), and zinc dust (100 gr.) The action began as soon as the materials were mixed. The products of the reduction were extracted from the zinc oxide with alcohol, benzene, and other solvents. Such substances as azoxybenzene and azoxynaphthalene were prepared by this method. Solutions of sodium chloride, potassium carbonate, potassium acetate, and other salts could be used in place of calcium chloride.

CHAPTER XX

PREPARATION OF SALTS

SECTION I.—GENERAL REMARKS

THE preparation of salts from acids and bases can be effected in so many ways that nothing like a complete account of the possible methods can be given here. Some of these are so well known that they require no description. They will be used as a matter of course whenever they are applicable.

1. Salts of Acids.—All acids which are insoluble in water can be dissolved by addition of caustic soda, caustic potash, or ammonia. Substitution products of the last are seldom employed, although Kleberg (*Ann.* **263**, 285) used phenylhydrazine on one occasion. It must be noted however that many salts are insoluble in strongly alkaline solutions.

Where the acid is soluble in water it can be converted by alkalis into the corresponding salts, and an excess of lime or baryta can be precipitated by means of carbon dioxide. If the quantity of the acid is known, the proper proportion of the alkali can be added at first. If the quantity of the acid is unknown and the acid can displace carbon dioxide, then the solution may be shaken with an insoluble carbonate till neutrality is reached. Barium and calcium carbonates are most frequently used for the purpose, although the carbonates of lead, silver, and other metals may be employed. If the acid dissolves oxides, lead oxide, moist silver oxide, and similar substances are applicable. Potassium and sodium carbonates are less used for this purpose, as it is difficult to determine the point when the acid is neutralised without the aid of standard solutions and titration.

The behaviour of solutions towards litmus and other indicators does not always give reliable information. Thus Ost (J. pr. Ch. **127**, 183) found that even the acid salts of pyromeconic acid of the formula, $C_5H_3O_2 \cdot OM + C_5H_3O_2 \cdot OH$, showed an alkaline reaction, and Pinner and Wolfenstein (Ber. **24**, 64) stated that an oxynicotine prepared by them had the properties of a base while exhibiting a feebly acid reaction.

Many organic acids resemble carbonic acid in giving no salts with weak bases. In one such case Altmann (Dissert. Neisse, 1874) evaded the difficulty by preparing the potassium salt of saccharic acid, mixing it with the calculated amount of aniline hydrochloride, and distilling the mixture, his object being to study the decomposition products of the saccharate of aniline.

2. Salts of Bases.—Bases soluble in water, alcohol, ether, and other solvents can be converted into neutral or acid salts by the addition of the proper acids. Thus Bernthsen (Ber. **16**, 2,235) prepared the neutral sulphate of amidodimethylaniline by mixing a known quantity, dissolved in ether, with an ethereal solution of the calculated amount of concentrated sulphuric acid. Under these circumstances the neutral salt was precipitated at once. Excess of sulphuric acid gave rise to the poorly crystallising acid salt.

Sulphuric acid is preferable to hydrochloric acid in such cases, as sulphates usually crystallise well while the hydrochlorides have a tendency to acquire a brown colour. Carbonic acid has no action on the majority of bases. The carbonate of tetrahydroquinoline, discovered by Bamberger (Ber. **22**, 354), for example, is exceptional.

Lellmann (Ann. **263**, 286) describes a method of determining the affinity coefficients of many organic bases, and another method has been worked out by Fuchs (M. f. Ch. **9** 1,132).

3. Precipitation of Salts Soluble in Water.—Salts which are soluble in water are frequently precipitated by means of alcohol or some other liquid in which they are not soluble. Hydrochlorides are often obtained by leading hydrochloric acid into a solution of the base in absolute ether or benzene (Ann. **256**, 290). In other cases the hydrochloride is insoluble in strong hydrochloric acid, and can therefore be thrown down from solution in water by leading in a stream of hydrochloric acid gas until precipitation is complete. Sometimes this method is modified by adding strong hydrochloric

acid to the solution and evaporating on the water bath until, with increasing concentration, the salt gradually separates out.

Oxalates and *picrates* of organic bases are very often prepared because they are usually difficultly soluble and have excellent power of crystallisation. For example, the alcoholic solution of the base is neutralised with a similar solution of oxalic acid, and the oxalate is precipitated by adding ether.

The use of these salts may be illustrated by reference to the case of a base obtained by condensation from *m*-phenylene diamine and *œnanthol* by Miller and Gerdeissen (Ber. **24**, 1,732). The platinum double salt was non-crystalline, and purification was finally attained by preparing the picrate. The oily base was dissolved in alcohol, and a strong alcoholic solution of picric acid was added. After the mixture had remained at rest for a considerable time a mass of crystals permeated with oil separated out. By washing with cold acetic acid and recrystallising from the same solvent the salt was finally obtained as a crystalline powder. The base itself, dihexyldi-*amylphenanthroline*, could then be freed from combination, and obtained from alcohol in snow-white crystals.

As a rule, salts are more soluble in hot than in cold water. The most remarkable exception to this rule is probably zinc xylidate (Jacobsen, Ber. **10**, 859). At 0° 100 parts of water dissolve nearly 36 parts, while at 100° they dissolve only 0·75 parts, and at 130° almost exactly 0·5 parts of the salt. A similar phenomenon has been noticed in the case of liquids. Kekulé and Zincke (Ann. **162**, 145) found that 100 parts of water at 13° dissolved 12 parts of paraldehyde. On warming the solution it became cloudy at 30°, and at 100° about half of the substance had separated out.

4. Water of Crystallisation.—The amount of water of crystallisation is determined usually by warming a weighed portion of the salt in a drying oven or *in vacuo* until the water is driven off. The substance may also be exposed *in vacuo* at the ordinary temperature.

The water of crystallisation in salts is frequently determined by the elementary analysis, especially when, during the ordinary method of heating, decomposition sets in before constancy in weight has been obtained.

The loss of water of crystallisation is in many substances accompanied by a change of colour. Thus the steel-blue needles of *p*-azotoluenenaphthylamine sulphate, on being warmed to 105° (Ber. **12**, 229), lose three molecules of water and become green.

Jacobsen (Ber. **15**, 1,854) determined the proportion of water of crystallisation in acids by titration with normal caustic soda. Bases might be treated in the corresponding manner.

5. Determination of the Solubility of Salts.—The determination of the solubility of salts is very valuable (Limpricht, Ber. **8**, 350) for deciding as to the identity or non-identity of similar, and particularly of isomeric, substances. The importance of this property is especially great in the case of salts whose melting- or boiling-points cannot be observed, whose crystalline form is not sufficiently well developed to permit of exact study, or whose water of crystallisation is variable in amount.

V. Meyer's method (Ber. **8**, 999) for determining the solubility of a substance is as follows: The material under examination is dissolved in hot water in a test tube holding 50–60 cc. The tube is placed in a large beaker of cold water, and the contents are stirred vigorously with a sharp-edged glass rod until they have attained the temperature of the water. After the whole has remained at rest for two hours the water is stirred and its temperature taken. The contents of the tube are then once more stirred violently, and a quantity sufficient for the determination is poured through a folded filter into a tared crucible provided with a lid. The solution is weighed, and the amount of dissolved substance determined either by evaporating the solvent and weighing the residue, or in any other suitable manner.

To determine the solubility of a substance in hot solvents, the boiling saturated solution is filtered into a tared flask through an ashless filter paper placed in a warm funnel. After the flask has remained closely stoppered for three to four hours the stopper is removed momentarily to equalise the pressure, and the flask with its contents is weighed. The solution is then evaporated in a water bath, and the residue finally dried in a drying oven. A third weighing gives the amount of solid material which the solution contained.

When it is desirable to measure the solubility at a definite temperature, a quantity of the substance is taken and covered with the solvent previously heated to the desired temperature, an amount of the latter being chosen which is insufficient to dissolve all the substance. The flask is then placed in a bath, and shaken periodically during several hours, the temperature meanwhile being maintained at the proper point. The subsequent treatment is the same as before.

6. Precipitation by Alcohol and Ether.—As has been mentioned, many salts which are soluble in water are insoluble in alcohol, so that they can be precipitated by addition of the latter to a water solution. The inverse of this however is very unusual. It was noticed by Hemilian (Ber. **16**, 2,364) in the case of barium salt of methyltriphenylmethane carboxylic acid. This salt is almost insoluble in water, but is rather soluble in 70 per cent. alcohol, and can be obtained in crystalline form from such a solution. Strecker (Ann. **67**, 4) observed that barium cholate was more soluble in alcohol than in water.

Salts which are soluble in alcohol can usually be precipitated by ether or petroleum ether. It is very unusual to find organic salts, especially those containing heavy metals, dissolving in the latter substances, although as early as the thirties Gusserow (Ann. **35**, 197) noticed that lead oleate was easily soluble in ether. The property of dissolving in ether seems to be characteristic of many of the salts of the oleic acid series. Thus Krafft and Beddies (Ber. **25**, 483) found that the barium salts of bromostearylene acid and several of its homologues were soluble in this medium. Such salts are on this account valuable for effecting separations.

7. Double Salts of Bases.—Many organic bases, including alkaloids (M. f. Ch. **9**, 511), form compounds with salts of heavy metals which are practically insoluble in water. Many years ago Hofmann (Ann. **47**, 56) recorded that "cyanol," now known as aniline, gave a green precipitate with solutions of cupric sulphate consisting of a compound, $(C_6H_5NH_2)_2 \cdot CuSO_4$. Later Schiff (Ann. Suppl. **3**, 348) prepared a double salt of ethylideneaniline and mercuric chloride. It may be also mentioned that quinoline forms with cobaltous chloride a compound of the composition, $CoCl_2 \cdot 2C_9H_7N$ (Ber. **23**, 434).

The relative insolubility of these compounds in water often suggests the best *method for the isolation of the base* concerned. Thus Kossel (Z. physiolog. Ch. **5**, 155) separated hypoxanthine from a solution obtained by boiling nuclein for forty hours, by adding ammonia and silver nitrate, when a compound of hypoxanthine with this salt was precipitated.

Such compounds are usually insoluble in water, but they can generally be recrystallised from alcohol to which a little acid has been added. The last-mentioned compound of hypoxanthine is best purified by crystallisation from hot nitric acid (sp. gr. 1.1),

Lachowicz (M. f. Ch. **10**, 884) states that of all salts nitrate of silver has the greatest power of uniting with bases. He ascribes this power in general to the "residual energy" of the acid.

Phospho-molybdic acid in acid solution precipitates all alkaloids and organic basis containing nitrogen (Sonnenschein, Ann. **104**, 45). The reagent is prepared by precipitating ammonium molybdate with sodium phosphate, dissolving the well-washed precipitate in warm soda solution, evaporating the solution to dryness, and igniting the residue until the ammonia is completely expelled. If the molybdic acid should be partially reduced by this treatment, the mass is moistened with nitric acid and ignited again. The dry residue is then warmed with water, nitric acid is added to strong acid reaction, and more water added so as to produce 10 parts of solution from 1 part of the solid residue. The resulting solution is golden yellow, and when ammonium bases, alkaloids, or salts of these are added to portions of it precipitates are formed at once. When these are exposed to the prolonged action of the hydrates or carbonates of the alkaline earth metals, the bases are set free, and salts of the metals with phospho-molybdic acid are formed. Barium carbonate is the most convenient substance to use for this purpose.

Phospho-tungstic acid may be used in a precisely similar manner.

As an example of the use of this method Pellacani's (A. Path. Pharm. **16**, 442) preparation of nigelline may be described. The powdered seeds of the fennel flower (*nigella*) were extracted with 50 per cent. alcohol, and the liquid was precipitated with basic lead acetate. The precipitate, consisting of lead salts of vegetable acids, was removed by filtration, the excess of lead precipitated by means of hydrogen sulphide, and the solution concentrated at a gentle heat. Extraction with ether next removed a fluorescent substance along with traces of ethereal oils. After complete elimination of the extracting agent, sulphuric acid was added to acid reaction, and then phospho-tungstic acid. The resulting copious precipitate was collected on a filter, washed, and decomposed by mixing with water and barium hydroxide. The free alkaloid dissolved in the water. The excess of barium was removed with carbon dioxide, and the solution concentrated. Hydrobromic acid was finally added to the syrupy residue, and crude nigelline bromide crystallised out in the course of forty-eight hours.

Schulze and Steiger (Z. physiolog. Ch. **11**, 44) obtained arginine from lupine seeds, which had been allowed to germinate in the dark for two weeks, in

the following manner: The dried and finely powdered cotyledons were first extracted with water. The extract was strained through a cloth and precipitated with tannic acid, and then, without previous filtration, with lead acetate. The lead was moved from the filtrate with sulphuric acid, and, after renewed filtration, a solution of phospho-tungstic acid was added. A large quantity of a bulky precipitate, which settled very slowly, was formed, and was removed by filtration and washed with slightly acidified water, being somewhat soluble in pure water. It was next pressed between sheets of filter paper to remove as much of the mother-liquor as possible, and thoroughly ground in a mortar with calcium hydroxide and water, with addition of a little barium hydroxide. The filtrate was then freed from calcium and barium by a current of carbon dioxide, neutralised with nitric acid, and evaporated almost to a syrup. On standing some time the solution deposited a large amount of nitrate of arginine in crystalline form.

Hofmeister (Z. physiolog. Ch. **2**, 311) decomposed a phospho-molybdate precipitate with lead carbonate, and removed the metal which went into solution from the filtrate with hydrogen sulphide.

Fischer (Ann. **190**, 184) has found that many, if not all, bases can be precipitated as difficultly soluble substances in the form of *salts of hydroferrocyanic acid*. Thus dimethylaniline and diethylaniline may be precipitated from very dilute acid solutions by potassium ferrocyanide, aniline itself from concentrated solutions only. These salts, when suspended in water, are instantly decomposed by alkalis and the bases set free.

This method is very convenient for separating bases from resinous material and for obtaining the last portions of bases which are but slightly soluble in water (Ber. **16**, 714). It can even be used for the quantitative precipitation and separation of alkaloids. Thus strychnine can be determined in presence of brucine as acid ferrocyanide of strychnine. Beckurts (Ann. Pharm. **1890**, 347) has investigated a large number of such compounds.

Wurster and Roser (Ber. **12**, 1,827) found that the salts of hydroferrocyanic acid examined by them were more soluble than those of hydroferrocyanic acid. The former are sometimes acid salts and sometimes neutral, the latter are always acid salts. The determination of the water of crystallisation has to be conducted with caution, as many of the substances decompose more or less even at 100°.

It is also worth notice that alkaloids can usually be precipitated as *periodides*, and as *double salts with cadmium iodide, bismuth*

iodide, and other similar compounds. And their salts—not merely the bases themselves—have frequently the property of forming with other salts more or less insoluble double salts.

Double compounds with the salts of the noble metals, such as gold chloride, platinum chloride, and mercuric chloride, have long been known. The first double salt with zinc chloride was prepared by Pettenkofer (Ann. **52**, 97), and since then almost all metallic chlorides have been used for preparing such substances. Where it is necessary and is found to be possible they may be purified by recrystallisation. Details will be given below, under the respective metals. Sometimes the same pair of substances yields double salts of different composition according to the proportions of the ingredients used.

8. Obtaining Acids from their Salts.—In releasing acids from a state of combination, a mineral acid is added to the solution of the salt, when the organic acid either falls out as a precipitate or can be extracted from solution by a suitable agent. If the latter method fails, the solution is evaporated to dryness, and the residue extracted with alcohol or other solvent. If an excess of mineral acid is to be avoided, tropaoline is added to the water solution. The smallest trace of free mineral acid changes the colour, while organic acids have no effect.¹

If the acids are liquids and soluble in water, and can be distilled unchanged, they may be obtained free from water by decomposing their salts with dry hydrogen sulphide or hydrochloric acid. With the help of the former, dry formic acid can be prepared from dry lead formate. By the action of the latter Wallach (Ber. **9**, 1,213) made dichloroacetic acid from the dry potassium salt. The salt was placed in a long combustion tube, which rested in a furnace standing in an inclined position. One end of the tube was connected with a generator of hydrochloric acid, and the other with a condenser. The gas was at first absorbed rapidly. As soon as it began to issue from the condenser the tube was cautiously warmed, and the acid distilled off in a slow stream of hydrochloric acid. The yield was almost quantitative.

9. Obtaining Bases from their Salts.—Bases are usually set free from salts by means of alkalis or alkaline carbonates. Thus

¹ Cf. Chap. XXII. § 3.

pseudo-ephedrine (Ber. **22**, 1,823) is made by adding potassium carbonate to a solution of the hydrochloride and extracting with ether. It appears in crystalline form as the ether evaporates. Dragendorff (A. Path. Pharm. **7**, 57) separated delphinine from the acid solution, in which it was finally isolated from the vegetable extract, by adding powdered sodium bicarbonate to distinct alkaline reaction and subsequent extraction with ether. Neutral alkali carbonates and caustic alkalis could not be used on account of the instability of the alkaloid. Buchka (Ber. **24**, 253) obtained cytisine by decomposing the tannate found in the vegetable extract with litharge.

Many bases can be set free with sodium acetate. Thus Bischler (Ber. **22**, 2,802) added an excess of this salt to a warm solution of *o*-nitrophenylhydrazine in water, and the base was deposited quantitatively in crystalline form.

Many solid bases take the form of an oil when set free in water solutions of their salts, and effectually resist every effort to change them to the solid form. In such cases, if the base can be distilled unchanged, it is mixed in the form of the salt with sodium carbonate and distilled in a retort. Under these circumstances the base passes over free from water, and solidifies in the receiver. This process is necessary in the case of *m*- and *p*-phenylene diamine, for example (Ber. **7**, 1,531).

10. Preparation of Salts by Double Decomposition.—When it is desired to prepare insoluble salts of acids by double decomposition it is best to use salts like barium and magnesium acetates, as the precipitates are less likely to be at all soluble in the dilute acetic acid produced by the action than they would be in the nitric or hydrochloric acid set free from salts like silver nitrate. Or all presence of free acids may be avoided by adding the reagents to solutions of the sodium, potassium, or ammonium salts of the organic acids.

When a mixture of acids or of bases is present in a solution a separation may be effected by fractional addition of the reagents. Thus, if we have a mixture of sodium salts of different acids, the addition of an insufficient amount of a mineral acid will set the weakest acid free first.

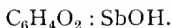
The reader may here be reminded of the use of dextrotartaric acid and laevotartaric acid for separating synthesised bases into the optically active components. This method was used by Ladenburg (Ann. **247**, 86) in his study of synthetic coniine. Fischer's work

(Ber. **23**, 2,611), in which he obtained optically active acids with several asymmetric carbon atoms, or altered the rotatory power of such acids, by the help of quinoline, strychnine, and similar alkaloids should also be mentioned.

SECTION II.—PREPARATION AND ANALYSIS OF SALTS.

11. Salts of Organic Acids containing Metals.—Neutral *ammonium salts* are obtained by dissolving the acid in excess of ammonia and allowing the solution to evaporate either in the air or in the desiccator over sulphuric acid.

Antimony salts and antimonyl compounds are seldom prepared if we except tartar emetic. Causse (C. R. **114**, 1,073) describes an antimonyl compound with catechol with the formula



In *barium* salts the metal is determined as BaSO_4 .

When the barium salt is soluble in water, it is usually prepared by dissolving the acid in excess of baryta water and removing the excess of barium with carbon dioxide. Insoluble salts are obtained by double decomposition.

It is unusual to obtain acid salts, although König (Ber. **22**, 787) made one, having the composition $(\text{C}_{10}\text{H}_5 \cdot \text{OH} \cdot \text{COOH} \cdot \text{SO}_3)_2\text{Ba}$, by precipitating a warm solution of oxynaphthosulphonic acid with barium chloride. The neutral salt, $\text{C}_{10}\text{H}_5(\text{OH})\left\langle \begin{smallmatrix} \text{COO} \\ \text{SO}_3 \end{smallmatrix} \right\rangle \text{Ba}$, he formed by treating the acid with barium carbonate. Acid barium salts of complicated composition, such as that from glycuronic acid (Z. physiolog. Ch. **3**, 442), occur but seldom.

For the conversion of potassium salts into soluble barium salts Berthelot (C. R. **109**, 227) recommends the precipitation of the potassium with hydrofluosilicic acid, addition of barium carbonate to the filtrate, and renewed filtration. Instead of this the theoretical amount of a normal solution of sulphuric acid can be added, and the potassium sulphate precipitated by adding ten times its volume of absolute alcohol to the mixture. The filtrate can then be treated with barium carbonate either directly or after the alcohol has been removed by distillation.

Cadmium salts usually crystallise well. They were used by E. Fischer (Ber. **24**, 4,217) in the purification of ribonic acid. The determination of the cadmium by precipitating solutions of

its salts with alkaline carbonates, and ignition of the precipitates gives very variable results. On account of the volatilisation of some of the metal from the part of the precipitate remaining on the filter paper, the proportion of cadmium found is too low. According to Barth and Hlasiwetz (Ann. **122**, 104), better results are obtained by covering the salts with fuming nitric acid and evaporating on the water bath. This operation is repeated till the organic part of the substance is completely destroyed, and the dry residue is carefully heated, and the resulting oxide strongly ignited.

In *calcium* salts the metal is determined as CaSO_4 .

These salts, like those of barium, are frequently made by dissolving the acid in lime water and precipitating the excess of lime with carbonic acid. As the latter retains some of the carbonate in solution as bicarbonate, the solution must be thoroughly boiled before filtration to convert this into the insoluble neutral carbonate. Where boiling is inadvisable the plan used by Schulze and Steiger (Z. physiolog. Ch. **11**, 47) may be followed, and the solution exposed to the air for twenty-four hours in an open dish in order to permit as complete a change into the insoluble carbonate as possible.

According to Destrem (Ann. Ch. Ph. [**5**], **27**, 7), the calcium salts of the primary alcohols may be prepared by heating the latter in a dry condition with calcium oxide at $120-130^\circ$. These salts, like the corresponding barium salts, which are prepared by the same method, are unstable in contact with water.

According to Niederhäusern (Ber. **15**, 1, 120), the calcium salts of the phenols are formed by acting on finely powdered slaked lime with a slight excess of the phenol dissolved in ether. The mixture is frequently shaken during twenty-four hours, the ether is distilled off, and the pasty material which remains is evaporated to complete dryness while being constantly stirred. The granular substance which remains is almost completely soluble in water.

Acids can be obtained from their calcium salts by E. Fischer's method (Ber. **24**, 1, 842). The powdered salt is thrown into a dilute solution of oxalic acid containing little more than the calculated amount of acid, and the small excess is afterwards removed by adding calcium carbonate.

In *cobalt* salts the metal is determined as such, the oxides being reduced to metallic cobalt by ignition in a stream of hydrogen.

In *copper* salts the metal is determined as Cu_2S , obtained by ignition with sulphur in a stream of hydrogen.¹

Liebermann and Kühling (Ber. **24**, 410) used the solubility of the copper salt of hygrinic acid in chloroform as a means of purification by dissolving it in chloroform, precipitating with ether, and repeating the process several times.

Copper salts likewise give double compounds with organic bases. Thus Förster (Ber. **25**, 3,421) prepared a compound of copper acetate with pyridine, $\text{Cu}(\text{C}_2\text{H}_3\text{O}_2)_2$, $4\text{C}_5\text{H}_5\text{N}$, by grinding finely powdered copper acetate with excess of pyridine.

Organic compounds of copper occur which are somewhat volatile, and cannot therefore be ignited either in the air or in a stream of oxygen without loss of copper. Such substances may be treated by Walker's method (Ber. **22**, 3,246), by first warming them gently in a Rose's crucible in a stream of hydrogen sulphide until the organic body is volatilised, and then finishing the analysis in a stream of hydrogen.

In the case of *gold*, double salts are almost the only ones prepared. They are constituted according to the formula, $\text{B} \cdot \text{HCl}$, AuCl_3 , in which one molecule of the hydrochloride of the base is united with one molecule of auric chloride. The percentage of gold is ascertained by ignition of the salt.

When a determination of the chlorine is also required, Scheibler (Ber. **2**, 295) dissolves a weighed quantity of the gold salt in water, or suspends it in water if it is insoluble, and introduces some magnesium ribbon. The gold is deposited in the metallic state, and hydrogen is evolved. The operation is carried out in the cold, or, in the case of less soluble substances, in the water bath. It is sometimes advisable to acidify the liquid. The precipitated metal is washed by decantation and collected by filtration. The filtrate is set aside for the determination of the chlorine, and the metal is washed again with water containing some hydrochloric acid to remove all traces of magnesium or magnesium hydroxide. The same treatment holds also for platinum double salts.

Water of crystallisation is seldom found in gold double salts. Nicholson (Ann. **62**, 71) described the double chloride of gold and caffein as free from water; but Biedermann (Ar. Pharm. **1883**, 182) found that when the equivalent amount of auric

¹ The value of this old-established method has recently been contested by Uhl (Ber. **23** 2,153).

chloride was added to a warm solution of caffeine in dilute hydrochloric acid, the solution deposited on cooling almost all the double salt in the form of small plates, having the composition $C_8H_{10}N_4O_2 \cdot HCl, AuCl_3 + 2H_2O$. Schmidt (Ar. Pharm. **1883**, 664) has shown that synthesised caffeine exhibits almost the same behaviour.

In *lead* salts, the lead is determined as $PbSO_4$ by repeated evaporation with sulphuric acid.

Lewkowitsch (Ber. **24**, 653c) states that in preparing glyceric acid by the decomposition of its lead salt with hydrogen sulphide a certain amount of the lead always remains in solution. In this case it can be obtained quite pure by decomposing the calcium salt with oxalic acid.

In the case of *magnesium*, the salts are ignited and the residue weighed as MgO .

Kiliani (Ber. **24**, 343) confirmed the formula assigned to digitogenic acid by determining the magnesium in the crystalline salt. He moistened the acid with alcohol, and then added strong caustic potash until only a trace of the acid remained undissolved. To the filtered liquid he added so much water that the addition of a solution of magnesium nitrate (1 : 10) only produced a faint opalescence. Excess of this reagent having been added, and the mixture having been left at rest for twenty-four hours, the magnesium salt of digitogenic acid crystallised out in a white mass, which was washed with cold water.

Gaze (Ar. Pharm. **1891**, 490) obtained the magnesium salt of propionic acid in crystalline form by dissolving the salt in alcohol and adding acetic ether to the solution.

Manganese salts are analysed by ignition and subsequent heating of the residue with ammonium nitrate. The metal remains behind as Mn_2O_3 .

Mercury salts are not very frequently made. The metal is determined as sulphide.

Heuser and Stöhr (J. pr. Ch. **150**, 437) describe a double salt of α -dimethyldipiperidyl, having the formula $C_{12}H_{12}N_2 \cdot 2HCl + 6HgCl_2$. The usefulness of double salts of this nature for the separation of isomers among the pyridine bases was recognised by Ladenburg. Pure pyridine itself (Ann. **274**, 4) is obtained by dissolving commercial pyridine (20 gr.), which boils between 114° and 118° , in 10 per cent. hydrochloric acid (100 gr.), and adding a solution of mercuric chloride (135 gr.) in 1 litre of hot water. On cooling, the solution

deposits a double salt, which can be purified by recrystallising from boiling water, and melts at 178° . By distillation with caustic soda the base is set free again, and may be dried with solid caustic potash. It is finally distilled, and all passes over at 114° .

Nickel salts leave behind NiO on ignition.

Platinum double salts are probably more frequently prepared than any others. They are usually obtained by the addition of a solution of platinum tetrachloride to a solution of the hydrochloride of the base in water or alcohol. They generally appear as crystalline precipitates, or at least change into such in a short time. Thus Nietzki (Ber **16**, 467) mentions that when platinum tetrachloride is added to a solution of phenosafranine hydrochloride a red cheese-like precipitate is formed, which almost immediately turns into beautiful golden plates. In composition the salts correspond to the double chloride of platinum and ammonia, $\text{PtCl}_4 + 2\text{NH}_3 \cdot \text{HCl}$, the ammonia being replaced by the base in question. Double salts containing water of crystallisation are very uncommon. In this connection it may be mentioned that Baeyer (Ber. **12**, 1,322) found that the double salt of quinoline had the composition $(\text{C}_9\text{H}_7\text{N} \cdot \text{HCl})_2 \text{PtCl}_4 + \text{H}_2\text{O}$, and he also states that the platinum salt of synthetic picoline crystallises sometimes with and sometimes without water of crystallisation in a purely arbitrary fashion.

According to Zincke (Ber. **25**, 1,497), the double salt of platinum with isoquinoline crystallises with two molecules of water, $(\text{C}_9\text{H}_7\text{N} \cdot \text{HCl})_2 \text{PtCl}_4 + 2\text{H}_2\text{O}$. Andreocci (Ber. **24**, 955*c*) finds that when the chloroplatinate of 1-phenyl-3-methylpyrazol crystallises from hydrochloric acid containing excess of platinum tetrachloride it unites with three molecules of water. When 1-phenyl-3-methylpyrodiazolon is dissolved with platinum tetrachloride in fuming hydrochloric acid a double salt containing four molecules of water is obtained. Like many other similar double salts it cannot be recrystallised from water. On adding a very strong solution of platinum tetrachloride to phenylammeline, made into a paste with concentrated hydrochloric acid, and heating, Smolka and Friedrich (M. f. Ch. **11**, 7) found that the whole went into solution. But the crystals deposited on cooling were decomposed by water, so the substance was purified by adding alcohol to the warm solution, and afterwards washing the crystals with the same substance.

When it is desired to recover the base from the double salt, or to use the preparation of the latter as a means of purification, it is usual to suspend the salt in water and decompose it with hydrogen sulphide. The precipitated sulphide of platinum is very difficult

to filter, and unstable bases, like choline, are decomposed by such treatment. According to Schmiedeberg and Harnack (A. Path. Pharm. **6**, 14), the hydrochloride of choline can be best obtained from the platinum double salt by evaporating a solution of the latter to dryness with an equivalent amount of potassium chloride, and extracting the residue with alcohol. Gram (A. Path. Pharm. **20**, 119) recommends the decomposition of this salt with potassium chloride in the cold. The alcohol removes the hydrochloride of the base, and leaves the potassium chloroplatinate undissolved.

Bases which are volatile without decomposition can be isolated by distilling the double salts with sodium carbonate.

A few platinum double salts, varying from the type given above, are known. Thus Hofmann (Ber. **20**, 2,253) by treating the amidine of *o*-amidophenylmercaptan with hydrochloric acid and adding platinum tetrachloride to the resulting hydrochloride, without bringing it first into solution, obtained a salt crystallising in needles, which, after being washed with hydrochloric acid and dried, had the composition $C_8H_7N_3S \cdot 2HCl$, $PtCl_4$. The gold double salt had the normal composition, however, $C_8H_7N_3S \cdot HCl$, $AuCl_3$.

The platinum is determined by ignition. But in all cases where the composition of a base is determined solely by that of the platinum double salt an estimation of the chlorine must also be made. Wallach (Ber. **14**, 753) recommends the following method: The platinum salt is weighed out in a platinum dish, covered with a fresh concentrated solution of from one half to one gram of sodium in absolute alcohol, and evaporated on the water bath until a crystalline scale begins to be formed on the surface. The basin is then placed on a triangle, and the alcohol set on fire. The alcohol and alcoholate will now burn quietly without spurting or frothing provided fresh alcoholate was used to start with. The platinum salt is completely decomposed, yielding metallic platinum, while the chlorine all combines with the sodium. When the flame has gone out the vessel is heated for a short time longer over the naked flame. When it has cooled once more, the contents, consisting of sodium carbonate and chloride, platinum, and carbon, are washed into a beaker, acidified with nitric acid, and filtered. The chlorine can be determined in the filtrate. The platinum and carbon on the filter are restored to the platinum basin, and the platinum determined by ignition. The numbers for chlorine are very accurate. Those for platinum are often less satisfactory, but

amply suffice for the recognition of the proportion of platinum to chlorine in the salt.

According to Mylius and Förster (Ber. **24**, 2,439), the loss of metal in platinum determinations may be due to the formation of volatile carbonyl-platinous chloride, COPtCl_2 . In the heating of platinum double salts there is certainly opportunity for carbon monoxide and chlorine to interact with the chloride.

The recovery of the platinum from double salts is such a frequent task that the method devised by Duviliers (Ann. Ch. Ph. [5], **10**, 872) for the purpose may be described. The double salt (100 gr.) is thrown in portions into a boiling solution of sodium formate (50 gr.) and 25 per cent. caustic soda (50 cc.) in a litre of water. The reduction begins immediately, and after one hour's boiling the solution is filtered, and the platinum washed with warm water containing hydrochloric acid.

Potassium salts are usually obtained from the acids by treatment with caustic potash or potassium carbonate. From salts containing heavy metals they are made by double decomposition. If such salts are insoluble in water, they are covered with a solution of potassium carbonate, and the mixture is evaporated on the water bath, when the interaction takes place quantitatively.

To separate potassium chloride from an organic salt of potassium by extraction of the latter with alcohol, it is necessary to take almost absolute alcohol (Barth and Schmidt, Ber. **12**, 1,262), as otherwise much of the inorganic salt may go into solution also. When the organic salt is not sufficiently soluble in absolute alcohol, it is advisable to treat the aqueous solution first with silver sulphate to convert the potassium chloride into sulphate. The latter is practically insoluble even in 70 per cent. alcohol.

The potassium is always determined as K_2SO_4 by ignition with sulphuric acid.

König (Ber. **22**, 788) describes an acid potassium salt.

Silver salts are prepared by the general methods. In many cases it is desirable to apply the nitrate of silver in alcoholic solution; it dissolves in four parts of boiling alcohol (Gmelin, Handbuch, **3**, 624). Silver salts are almost always neutral and free from water, so that they are useful for determining the valency of acids and for similar purposes.

According to Königs and Körner (Ber. **16**, 2,153), carbon dioxide is frequently most easily removed by distilling the silver salts. This method is specially advantageous in treating acids which con-

tain a strongly acid hydroxyl group, besides the carboxyl, like the aromatic oxy-acids. For such purposes it is preferable to the distillation with bases of the free acids or their calcium salts. The above observers found that on distilling oxycinchonic acid with bases much charring took place; while on heating the silver salt (5 gr.) in a combustion tube in a stream of carbon dioxide, it yielded two grams of oxyquinoline and the charring was very slight.

Although in the case of inorganic acids, neither acid nor basic silver salts are known (Mendelejeff, Principles of Chemistry, Vol. 2, p. 396), a few acid salts of organic acids are met with. Thus Thate (J. pr. Ch. **137**, 157) prepared both the neutral silver salt, $C_{16}H_{12}N_2O_7Ag_2$, and the acid salt, $C_{16}H_{13}N_2O_7Ag$, of azoxy-*o*-phenoxy-acetic acid. Schmidt (Ar. Pharm. **1886**, 521) prepared both the neutral and acid salts of jervic acid with the formulae, $C_7H_2Ag_2O_6$ and $C_7H_3AgO_6 + H_2O$, respectively. According to Jeanrenaud (Ber. **22**, 1,281), a silver salt of tetrahydrodioxytetraphthalic acid with the unusual constitution, $C_6H_2(OAg)_2(COOAg)_2H_4 + 2H_2O$, can be prepared. Claus and Kohlstock (Ber. **18**, 1,849) prepared amarine-silver, $C_{21}H_{17}N_2Ag$, and found along with it large crystals of diamarine silver nitrate, $(C_{21}H_{18}N_2)_2AgNO_3 + H_2O$, when they allowed a solution of amarine and silver nitrate in dilute alcohol to remain for several weeks. Dimethylpyron carboxylic acid (Feist, Ann. **257**, 290) gives a salt of the composition, $C_8H_7AgO_4 + AgNO_3$, and diphenylpyron dicarboxylic acid (Feist, Ber. **23**, 3,733) gives likewise a salt containing nitrate of silver having the composition $(C_{18}H_{11}AgO_4)_2 + AgNO_3$.

Schmiedeberg and Meyer (Z. physiolog. Ch. **3**, 433) found that the silver salt of camphoglycuronic acid is represented by the formula, $C_{16}H_{23}AgO_8 + 3H_2O$, and Eckhardt (Ber. **22**, 276) prepared a silver salt of metaquinaldineacrylic acid having a composition represented by the formula, $C_{13}H_{10}NO_2Ag + 4H_2O$.

When organic salts of silver are ignited the metal remaining behind often contains carbon.

In *sodium* salts the metal is always estimated as Na_2SO_4 .

The fact that most organic sodium salts are soluble in alcohol, while sodium carbonate, as well as many other substances, inorganic and organic (albumens, &c.), are insoluble in it, suggests a method of obtaining sodium salts of organic acids which is of very wide application. The material under examination is treated with cold or warm caustic soda, and carbon dioxide is led into the filtrate to convert the sodium into carbonate. The solution is then evapor-

ated as far as possible in the water bath, and the residue extracted with 80 to 90 per cent. alcohol, when the organic sodium salt is obtained in almost complete purity.

Brühl (Ber. **24**, 3,390) prepared the sodium salt of camphor carboxylic acid by suspending the acid in water, and adding caustic soda until the solution showed a faintly alkaline reaction. After passing carbon dioxide through the solution he allowed it to evaporate *in vacuo*, and dissolved the residue in alcohol. On evaporating this alcoholic solution in like manner over sulphuric acid he obtained a crystalline powder, which was easily soluble in water, methyl alcohol, and chloroform. When the water solution was allowed to evaporate in the air, good crystals of the sodium salt were obtained.

Some sodium salts, like that of acetylendicarbodiazocetic acid (Buchner, Ber. **22**, 845), are nearly insoluble in cold water. König (Ber. **22**, 787) prepared the sodium salt, $C_{10}H_5(OH)(COOH)(SO_3Na)$, by adding a saturated solution of common salt in large excess to a warm solution of oxynaphthosulphonic acid, filtering off the precipitate, and recrystallising it from warm water.

In *strontium* salts the metal is determined as $SrSO_4$.

Tin double salts, especially in the form of double salts with stannous chloride, are of common occurrence. They appear in crystalline form from mixtures in which tin and hydrochloric acid have been used for the purpose of reducing.

Hofmann (Ber. **18**, 115) recommends the use of tin tetrachloride in the investigation of volatile bases. Thus he separated coneine from γ -coniceine by evaporating a mixture of their hydrochlorides until crystallisation set in, and adding stannic chloride to the concentrated solution. The use of excess of the inorganic salt was carefully avoided. The liquid soon became semi-solid from the presence of crystals of the double salt with γ -coniceine hydrochloride, while the corresponding compound with coneine, which does not crystallise, remained in the mother-liquor and appeared as a gummy mass on evaporation of the solvent. Pure γ -coniceine was isolated by further treatment. For the analysis, the salt, $2(C_{18}H_{15}N \cdot HCl) \cdot SnCl_4$, was dissolved in water, and the tin precipitated with hydrogen sulphide. The sulphide was then ignited in the air, and weighed as stannic oxide.

In *zinc* salts the metal is weighed as ZnO .

The zinc salts seem to be specially suited for assisting in the preparation of pure acids. Thus Hell and Rempel (Ber. **18**, 817)

made pure oxysuberic acid by neutralising an aqueous solution of the acid, as it is obtained in syrupy form, with ammonia, and precipitating with a concentrated solution of zinc sulphate. The zinc salt was collected on a filter, and decomposed in a porcelain dish with moderately strong sulphuric acid. The oxysuberic acid was insoluble in the solution of zinc sulphate, and was collected as a crystalline powder by filtration and recrystallised from ether. The same method was used by Bujard and Hell (Ber. **22**, 70) for the purification of oxylepargylic acid.

The zinc salts of isomeric acids frequently show characteristic differences. Thus, that from lactic acid from fermentation crystallises with $3\text{H}_2\text{O}$, that from sarcolactic acid with $2\text{H}_2\text{O}$, and that from ethylenelactic acid with $4\text{H}_2\text{O}$. The solubilities of these salts in water and in alcohol are likewise quite different.

Mekilow (Jahresb. **1885**, 1,350) even separated β - from γ -chloroxybutyric acid by means of the different solubility of their zinc salts in water.

Double salts containing zinc are also sometimes useful, as in the case of ethylenelactic acid, which Heintz purified by this means. The salts of this acid are hard to crystallise on account of their great solubility in water. But when Heintz (Ann. **157**, 294) divided a quantity of the impure acid into two portions, saturated one with quicklime and the other with zinc oxide and mixed them, part of the double salt was precipitated at once, and the rest came out of the mother-liquor on evaporation. From this salt, after recrystallisation, he removed the zinc with hydrogen sulphide, and the lime with an equivalent quantity of oxalic acid, and so obtained the acid in a pure condition. This appeared to be the only possible way of obtaining the pure acid from such a source.

For the preparation of bases in the form of sulphates from double salts with zinc chloride, a method used in manufactories (Ger. Pat. 46,438) may often be found useful in the laboratory. The zinc double salt with diamidocarbazol hydrochloride, for example, is mixed with sodium sulphate, and the sulphate of diamidocarbazol, which is but slightly soluble, crystallises out.

12. Salts of Organic Bases with Organic Acids.—Organic salts of organic bases are frequently prepared, as they often serve to characterise the acid or assist in its purification. Thus allocinnamic acid forms a salt with aniline (Ber. **25**, 951), which is insoluble in benzene, while the closely related hydrocinnamic acid is not precipi-

tated in benzene solution by aniline. E. Fischer (Ber. **24**, 3,624) found that talonic acid could be best purified by conversion into a salt with brucine. This salt was obtained by boiling a dilute solution of the acid in water, with a slight excess of brucine, for fifteen minutes, evaporating to a syrup, and allowing the residue to crystallise. The remaining water was removed by stirring with absolute alcohol and filtering. The salt was finally purified by recrystallisation from methyl alcohol.

13. Ignition of Explosive Salts.—The analysis of explosive salts may be conveniently discussed in closing this chapter. The violence of the action may be modified by mixing with sand, or recourse may be had to the conversion of the compounds into non-explosive ones by evaporating them with strong mineral acids, bromine water, or other reagents before the ignition. Thus Fischer (Ann. **199**, 303) decomposed potassium diazoethanesulphonate by evaporation on the water bath with dilute sulphuric acid, and could then ignite the residue without danger of explosion.

14. Determination of the Ash in Organic Matter.—The estimation of the amount of ash in organic substances containing salts is rendered difficult by the fact that by mere ignition in an open basin all the carbon is not removed. Small pieces of the latter are surrounded by the melting alkali salts, and are protected from incineration. Efforts to burn the charred matter by using ammonium nitrate (Gorup Besanez), oxygen, or by fusion with soda and potassium nitrate (Stahel) have the disadvantages that either loss by spurting is to be feared, or inconveniently large amounts of material are accumulated when the quantity of ash is itself large. Combustion with potassium nitrate alone does not give exact figures, for alkaline chlorides are somewhat volatile at the high temperature of ignition. And besides, even prolonged ignition up to six hours, as recommended by Graanboom (Dissert. Amsterdam, 1881), does not give a perfectly white ash.

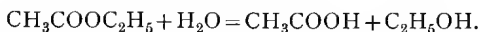
Bemmelen (Z. physiolog. Ch. **7**, 505) recommends the following method for escaping all these difficulties. The dry substance is first spread in small portions at a time in a thin layer in a platinum basin, and slowly charred with the heat of a small flame. As soon as the dry distillation has ceased, the carbonised mass is carefully broken up, stirred, and heated anew. It is possible in this way to carbonise the whole without any loss on account of swelling or

frothing. If several platinum basins are available, 50 grams can be worked up in this way in from one to two days. The whole mass of incinerated matter is finally thrown, in small portions at a time, into one or two platinum basins, or still better, into a Deville's platinum tray, and heated in a muffle such as Wiesnegg's. The material is kept at a dark-red heat, so as to avoid volatilisation of chlorides of potassium and sodium, and with a good draught the carbon is soon all consumed. If a portion should remain unburnt, the contents of the basin are washed into a beaker. The particles of carbon remaining undissolved by the water are collected on a filter and burnt in the muffle. Under such circumstances, being free from alkaline chlorides and phosphates, they easily burn to a white ash. By adding the residue from the evaporation of the water extract, the total ash is ascertained

CHAPTER XXI

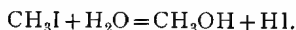
SAPONIFICATION

1. Saponifying Agents.—By saponification is meant the decomposition of an ester into its components, the acid and the alcohol, water being taken up in the process—



The water can be taken up directly under certain circumstances, as in Wilson and Gwynne's process for saponifying fats on a large scale. The fats are heated to 300° , and decomposed into fatty acids and glycerol by means of a current of steam heated to 315° .

Einhorn and Rassow (Ber. **25**, 1,397) obtained dihydroxyanhydroecgonine from the methyl ester by boiling it with water for twenty-four hours. The haloid compounds of alcohol radicals, which may be regarded as esters of hydrochloric acid, are decomposed on heating with water in accordance with this conception. Thus Niederist (Ann. **196**, 350) heated methyl iodide (26.2 gr.) with water (400 cc.) for eight hours in a closed vessel in the water bath. He found that the action took place almost quantitatively in the direction of producing methyl alcohol and hydriodic acid—



In the case of allyl iodide the substances required only to be boiled in a flask attached to a condenser.¹

¹ It may be worth mentioning here that Buchanan (Ber. **4**, 340) and Thomsen (Ann. **200**, 76) both showed that when monochloroacetic acid was boiled with water for several days, it was converted into glycollic acid and hydrochloric acid. Hölzer (Ber. **16**, 2,955) found later that this

In the laboratory saponifications, almost without exception, are conducted with the help of alkalis, sodium ethylate, lead or silver oxide, or acids. Quite recently aluminium chloride has been added to the list, and often renders the accomplishment of the object at the ordinary temperature possible.

2. Aqueous Caustic Potash or Soda.—These alkalis are much more frequently used than the hydroxides of the alkaline earths. Although the effects in both cases are nearly always identical, the former are preferred, because they can be applied in more concentrated solution.

The irregular way in which solutions of the alkalis boil is very inconvenient. When small quantities of very concentrated solutions are used—for example, one part of water to two parts of caustic potash, it is preferable to seal the substances up in a tube and heat at about 100° .

Bischoff (Ber. **24**, 2,015) dissolved potassium hydroxide (500 gr.) in water (200 cc.) in a basin, and added ethylacetosuccinic ether (400 gr.) in small portions at a time. The temperature was kept between 120° and 126° . The alcohol which was split off evaporated, and when the last portion had been added, about fifteen minutes after the first, the saponification was complete. The mass was diluted with water, and the solution rendered faintly acid with dilute nitric acid, and added to a solution containing lead nitrate (830 gr.). The precipitate was collected on a filter, and, while still moist, was decomposed with the calculated amount of sulphuric acid. The filtrate from the lead sulphate, when evaporated, deposited the ethylsuccinic acid. The yield was 50 per cent.

Baeyer (Ber. **14**, 1,743) found that indoxylic ether was best saponified by mixing with fused caustic soda at 180° . When the resulting yellow salt was treated with acids, indoxylic acid was thrown down as an almost colourless and hardly soluble precipitate.

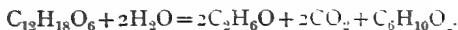
Very complex acids can sometimes be freed from combination in

action proceeded much more smoothly when pulverised marble (probably precipitated chalk would be still better) was added. Häussermann and Beck (Ber. **25**, 2,445) also converted *o*-nitrobenzyl chloride into *o*-nitrobenzyl alcohol (b.-p. 74°) by boiling with a dilute solution of potassium carbonate. From these facts it would seem that we might expect that the saponification of esters by water would be assisted by the presence of chalk, or that esters, which are easily split by caustic alkalis, might preferably be treated with this reagent.

esters without decomposition only by using alkali of definite concentration. For example, Guthzeit (*Ann.* **214**, 72) could obtain nothing but ethane tricarboxylic acid by saponifying ethane tetracarboxylic ether. Buchner, however (*Ber.* **25**, 1,158), boiled the ester (1 gr.) with caustic soda of sp. gr. 1.12 (4.5 cc.) for an hour and a half, neutralised, evaporated, and acidified the liquid, and finally extracted it with ether. He obtained, by evaporation of the extract, crystals of ethane tetracarboxylic acid.

As an example of saponification in the cold, it may be mentioned that Knorr treated diacetosuccinic ether (4 parts) with 25 per cent. caustic soda (5 parts) by allowing the mixture to remain for eight days. The decomposition into acid and alcohol was complete.

In the case of acids as complex as this, the strength of the caustic soda solution may have a considerable influence on the final result, even when the action takes place in the cold. Thus Knorr (*Ber.* **22**, 169) allowed the same ester to remain in the cold for several days with a slight excess of 3 per cent. caustic soda, and found that it broke up into alcohol, carbon dioxide, and acetylacetone, under these circumstances—



Paal prepared phenacylacetylacetic acid from the ester by letting the latter remain with 2 per cent. caustic potash for a few hours, and then filtering the solution into dilute sulphuric acid.

It will not always be convenient to isolate complex acids made from esters obtained by condensation of acetoacetic ether or malonic ether by simply precipitating the acid or extracting it from the acid solution with ether. For example, Conrad (*Ann.* **204**, 132) finds that the free acids from alkylmalonic ethers are best isolated by neutralising the alkaline mixture with acetic or hydrochloric acid, and precipitating the calcium salt of the organic acid by adding calcium chloride to the solution. This salt is usually crystalline, and can be best decomposed by adding the calculated amount of oxalic acid. The mixture is boiled for some time, and filtered from the insoluble calcium oxalate. The filtrate is evaporated to dryness, and the residue treated with ether to separate the acid from any oxalic acid which may still be present. The acid then remains as a white crystalline mass, and is purified by recrystallisation.

3. Alcoholic Caustic Potash.—When, as is often the case, the saponification is conducted by boiling with alcoholic caustic potash, the excess of the alkali can be precipitated for the most part by means of carbonic acid.

Paal and Hoffmann (Ber. **23**, 1,497), in trying to saponify iso-amylmalonic ether, $C_5H_{11} \cdot CH(COOC_2H_5)_2$, found that this could not be completely effected by alcoholic caustic potash, although boiling for several hours with an aqueous solution successfully accomplished the object. This is a very exceptional observation.

The author has found, after much experimentation, that the following is the best method of saponifying animal fat: The fat (1,250 gr.) is melted on the water-bath and poured into 96 per cent. alcohol (1.5 l.) which has previously been heated in a six litre flask. Caustic potash (400 gr.) is allowed to dissolve spontaneously in a little water, and this solution is immediately, while still hot, added in portions to the alcoholic solution of fat. The action is very violent, and as soon as the last portion of caustic potash has been added, and the whole has been shaken, the saponification is complete. This is seen from the fact that the product is completely soluble in water. No external heating is necessary during the operation.

4. Sodium Ethylate.—Kossel and Obermüller (Z. physiolog. Ch. **14**, 599) have found that, even in the cold, sodium ethylate is a capital saponifying agent, especially for fats. The process is described in a patent specification (Ber. **24**, 419c) as follows: The fat, cotton oil, spermaceti, Chinese wax or other similar substance is dissolved in benzene, petroleum ether, or ether, and sodium ethylate is added. Instead of this, alcohol and sodium can be used. After a few minutes an easily filtered precipitate is deposited which is chiefly composed of the soaps. When metallic sodium is used, its surface quickly becomes covered with this product and the mixture must be vigorously shaken so as to permit the action to continue. By this method, only 40–50 grams of sodium are required for a kilogram of cotton oil—that is, not much more than the calculated amount, and the operation occupies twenty-four hours. The same quantity of oil would have to be heated for twenty hours with excess of alcoholic caustic potash to attain the same result. The filtrate from the soap will, in this case, contain cholesterin and isocholesterin.

The same observers (Z. physiolog. Ch. **15**, 422) saponified phenyl salicylate (salol) by this method and obtained ethyl salicylate and phenol, and the former had to be finally decomposed with aqueous caustic soda. When sodium amyl alcoholate was used, the product was amyl salicylate. The method is therefore applicable only to fats.

According to Obermüller's view the glycerol ester and sodium

ethylate change first into the sodium salt of glycerol and the ethyl ester of the fatty acid. The former then reacts with the traces of water contained in the alcohol giving glycerol and sodium hydroxide. Finally this last easily decomposes the ethyl ester.

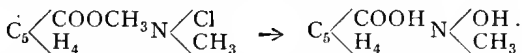
5. Baryta Water.—Esters may be saponified by prolonged boiling with baryta water in a flask connected with a condenser, or, if the temperature is not high enough, by heating the mixture in a sealed tube. The acid, which is found as barium salt at the conclusion of the action, is set free by a stronger acid and filtered off or extracted with ether as the case may be. If the barium salt itself is wanted, the excess of barium hydroxide can be precipitated with carbon dioxide and the filtrate evaporated until crystallisation begins. If, on the other hand, it is the alcohol whose isolation is desired, a case which seldom occurs, it may be distilled off or driven over with steam. Its separation from the distillate can be effected by adding a large amount of potassium carbonate or, if the nature of the alcohol permits, extracting with ether.

Bayer (Ber. **14**, 1,743) saponified the ester of ethylindoxyl acid by boiling with alcoholic barium hydroxide, and found that the free acid was deposited in white flakes when the liquid was acidified.

6. Lime Water.—The action of lime water is similar to that of baryta water. The inferior solubility of calcium hydroxide renders it less useful than the other.

7. Oxides of Lead and Silver.—As is well known, fats are decomposed when boiled with lead oxide and water. They decompose into the lead salt of the fatty acid and glycerol. The lead salts so obtained are known as lead soaps.

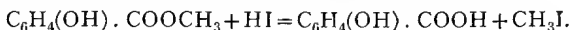
Hantzsch (Ber. **19**, 32) treated methyl nicotinate methchloride with silver oxide, and obtained the free acid,



so that here, not only was the chlorine removed, but the oxide saponified the ester as well.

8. Acids.—Not only do alkalis saponify esters, but acids like sulphuric and hydrochloric also split them into their components.

This is the more curious as these are the very agents used in forming esters out of acids and alcohols. The first observation in this connection was made by Lautemann (Ann. **125**, 13). He found that when hydriodic acid was led into methyl salicylate, salicylic acid was deposited and methyl iodide formed.



Then Gal (C. R. **59**, 1,049) stated that when esters were treated with hydrobromic acid they uniformly broke up into the acid and alkyl bromide. For example, methyl formate gave formic acid and methyl bromide.

Auwers and Meyer (Ber. **23**, 298) found that a mixture of the isomers, tetramethylsuccinic ether and trimethylglutaric ether, could not be separated by fractional distillation. He heated them with an equal volume of hydrobromic acid of sp. gr. 1.7 for ten hours at 100° in a sealed tube. The saponification was only partial, but, for the purpose of separation, was more advantageous than that with alcoholic potash.

Sapper (Ann. **211**, 179) has found that hydrochloric acid is the least suitable of the three for this work, which agrees with the fact that it is the most valuable for preparing esters. Hydrofluoric acid is still less effective.

The most convenient form in which this method can be applied is to saturate glacial acetic acid at 0° with hydrobromic acid and allow the ester to remain in contact with this solution for some time.

Baeyer (Ber. **23**, 1,625) states that the best way of saponifying acetyl-*p*-amidotriphenylcarbinol, in order to remove the acetyl group, is to dissolve the substance in glacial acetic acid and add the solution slowly to warm dilute sulphuric acid. The mixture is boiled till solution is complete, and finally the base is precipitated with ammonia.

Paal and Bodewig (Ber. **25**, 2,963) found that the benzoyl group also was best split off by the aid of sulphuric acid. They prepared orthonitrobenzyl alcohol by acting with sodium benzoate (1½-2 parts) on nitrobenzyl chloride (1 part) and decomposing the nitrobenzyl benzoate so obtained by boiling for three or four hours with 50 per cent. sulphuric acid.

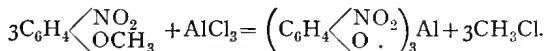
Bischoff and Mintz (Ber. **23**, 650) saponified ethylbutenyl tricarboxylic ether with sulphuric acid. Two parts of the ester were mixed with one part of water and one of concentrated sulphuric acid, and heated at 150-170°

in a round-bottomed flask connected with an inverted condenser until a drop of the mixture was completely soluble in alkali. The operation did not take much time, but secondary reactions always accompanied the saponification.

Stein (Ger. Pat. 61,329) states that when fat and oils are heated in a closed vessel with a 3 per cent. solution of sulphuric acid or of a bisulphate at 170–180°, a pressure of eighteen atmospheres is developed, and in the course of nine hours the substances are completely decomposed into fatty acids and glycerol.

9. Aluminium Chloride.—It has been shown by Hartmann and Gattermann (Ber. **25**, 3,531) that ethers of phenol and its derivatives, as well as esters, are very easily saponified by aluminium chloride. Besides the superior ease with which the operation can be carried out, this method presents the advantage over the use of hydriodic acid that it can be employed with substances like ethers of nitrophenols and ketonic derivatives of phenol which would be reduced by the other reagent.

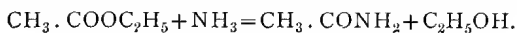
When the saponification is too energetic, carbon disulphide is used as a diluent. For example, orthonitroanisole (10 gr.) is dissolved in twice its volume of carbon disulphide and aluminium chloride (10 gr.) is added. The mixture begins to boil at once, as a result of the heat given out by the action. After the boiling has continued for half an hour, the flask being connected with a condenser from the first, the liquid separates into two layers. The upper one consists of carbon disulphide, and the lower of the aluminium salt of nitrophenol. After the former has evaporated, the residue is mixed with water and acidified with hydrochloric acid, and the free nitrophenol is driven over with steam. The yield is 90 per cent. of the theoretical.



10. Nonsaponifiable Esters.—To decompose the esters of tertiary alcohols it is sufficient to heat them at their boiling-points in a sealed tube for a considerable time. They break up into the acid and an unsaturated hydrocarbon. Quite at the other extreme however, we have esters which cannot be saponified at all. For example, Friedländer and Mähly (Ber. **16**, 850) found that dinitrocinnamic ether, $\text{C}_6\text{H}_4(\text{NO}_2) \cdot \text{CH} : \text{C}(\text{NO}_2) \cdot \text{COOC}_2\text{H}_5$, was not saponifiable either by alkalis or acids. The former decomposed

it and gave a brown-coloured product ; by the latter it was entirely split up into *p*-nitrobenzaldehyde and hydroxylamine.

It was first shown by Liebig (Ann. **9**, 130) that ammonia cannot take the place of the other alkalis in saponifying. Amides are formed by its action on esters. Thus acetic ether gives acetamide and alcohol.



CHAPTER XXII

PREPARATION OF SULPHONIC ACIDS.

1. Reagents Used.—Sulphonic acids are prepared by replacing hydrogen atoms by the group SO_3H . The reagents used for the purpose are the following :

Concentrated sulphuric acid.

Acid of composition H_2SO_4 .

Fuming sulphuric acid.

Sulphuric acid with phosphorus pentoxide or potassium bisulphate.

Sulphuryl oxychloride SO_2HCl .

Potassium or sodium bisulphate.

Potassium or sodium pyrosulphate.

Alkaline sulphites and bisulphites.

Carbysulphate.

Bisulphates and alkylsulphates of bases.

2. Concentrated Sulphuric Acid.—Even in the cold sulphuric acid interacts with many substances, producing sulphonic acids. For example, it had been generally accepted on the authority of Laurent that phenol and sulphuric acid gave a phenyl ester, but Kekulé (Z. Ch. **1867**, 199) showed conclusively that when equal parts of phenol and sulphuric acid were allowed to remain for several days in contact with each other, two phenolmonosulphonic acids were formed. This was a brilliant confirmation of the theory of the constitution of the aromatic bodies which he had published just before.

Most usually, however the action is assisted by heating. Thus Michel and Adair (Ber. **10**, 585) found that benzenesulphonic acid

was best prepared by gently boiling a mixture of equal volumes of benzene and sulphuric acid for twenty or thirty hours in a flask attached to a condenser. Four-fifths of the benzene went into solution during the process.

The *temperature* at which the operation is carried out has an important influence on the position which the sulphonc acid group will occupy in the aromatic ring. For example, when naphthalene (4 parts) is moderately heated with concentrated sulphuric acid (3 parts) in such a way that a part of the hydrocarbon remains unchanged, the product is α -naphthalenesulphonic acid. But when equal parts of the materials are heated at 200° , β -naphthalenesulphonic acid is formed.

Sempotowsky (Ber. **22**, 2,663) states that ethylbenzene is soluble with difficulty in concentrated sulphuric acid, but that it dissolves easily in the warm acid or in fuming sulphuric acid, giving two sulphonc acids. The following method, however, gives the *p*-sulphonic acid alone, and thus avoids the necessity of separating the isomers. The ethylbenzene is heated to the boiling point, and an equal volume of concentrated sulphuric acid is allowed to flow slowly into it, the mixture being vigorously shaken during the process. When the light yellow solution is cold, the sulphonic acid is mostly precipitated by adding ice-cold water to it. The remainder can be secured by using barium carbonate.

When quinoline is treated in the ordinary way only *o*- and *m*-quinolinesulphonic acids are formed. To obtain the *p*-compound the quinoline (10 parts) must be heated to $275-280^{\circ}$ with concentrated sulphuric acid (70 parts) in a sealed tube for twenty-four hours. The operation does not proceed further than the formation of the monosulphonic acids in the absence of sulphuric anhydride.

Nietzki (Ber. **15**, 305) stirred pulverised β -naphthol (1 part) with concentrated sulphuric acid ($1\frac{1}{2}$ -2 parts) and warmed the mixture slightly, obtaining a crystalline mass of naphthyl sulphate $C_{10}H_7O SO_3H$. On the other hand, Schaeffer (Ann. **152**, 293) heated the same materials on the water bath and found that under these circumstances naphtholsulphonic acid $C_{10}H_6(OH)SO_3H$ was formed.

In treating acids it is sometimes advantageous to use the potassium salt as the starting point. And similarly in the case of bases it is often helpful to the action to use a salt instead of the free base (cf. § 5).

The termination of the operation is usually recognisable by the

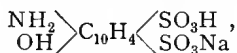
fact that a drop of the product is completely soluble in dilute alkali.

3. Isolation of the Products.—The strongly acid liquids obtained as above are worked up somewhat as follows .

The solution is mixed with half its weight of ice, and by this treatment many sulphonic acids crystallise out at once (Ber. **15**, 1,854) ; or the liquid is poured on to three times its weight of ice or into water containing a considerable amount of ice. The resulting dilute solution is neutralised with calcium or barium carbonate and filtered to remove the precipitated sulphate. The most active form of lime-water is made by placing quicklime in hot water. The calcium salts of sulphonic acids are usually soluble and crystallise when the solution is evaporated. If an insoluble barium salt of a sulphonic acid is mixed with the barium sulphate, the precipitate is washed and treated with dilute sulphuric acid. The sulphonic acid can then be extracted with ether or converted into a salt as may be most convenient.

If the acid liquid is neutralised with lead hydroxide or carbonate the lead salt of the sulphonic acid remains in solution. When the lead sulphate has been removed by filtration, the dissolved metal can be separated by means of hydrogen sulphide and an aqueous solution of the free sulphonic acid obtained.

Sometimes the acid solution is neutralised with soda and evaporated to dryness. The sodium salt of the sulphonic acid can usually be extracted from the residue with alcohol. Or salt is added to the neutralised solution to throw down the sodium salt. Thus Witt (Ger. Pat. 49,857) added common salt to the solution of the acid sodium salt of amido- β -naphtholdisulphonic acid



and obtained the substance at once in crystalline form.

This process, with which we have long been familiar in technical work, has recently been recommended for use in the laboratory by Gattermann (Ber. **24**, 2,121). He gently warmed benzene, for example, with slightly fuming sulphuric acid, converting it into the monosulphonic acid, and poured the mixture into twice its volume of cold water. Pulverised salt was added and shaken with this liquid until no more was dissolved. When this point was reached the solution was cooled. The benzenesulphonate of sodium crystallised out in a short time, and the crystals were filtered off and

washed with a solution of salt. The yield was almost quantitative. If the removal of all the salt is desired, the substance can be recrystallised from absolute alcohol. He prepared in a similar manner the sodium salts of mesitylenesulphonic acid, *m*-sulphobenzoic acid, phenoldisulphonic acid, and many other compounds of this class.

After operations like this, the amount of sulphuric acid which remains unused can be determined by titration, an azo-dye being used as indicator (Ann. **219**, 210), and the addition of barium carbonate or other neutralising agent can then be regulated so that, after filtration, the free sulphonic acid remains in solution.

Lunge ("Sodaindustrie" **1**, 40) states that, for ascertaining the presence of sulphuric or any other strong acids, dyes of this class, such as amidoazobenzene (aniline yellow) and tropaöline, form the best indicators. They are not affected by salts of metals, but are sensitive to the presence of the least trace of a strong acid, and are quite indifferent to such substances as carbon dioxide, hydrogen sulphide, and acetic acid (cf. Chap. XX., § 8).

4. Sulphuric Acid containing 100 per cent. of H_2SO_4 .—Acid of this strength is often very effective in preparing sulphonic acids. It is best made, according to Lunge, by mixing ordinary sulphuric acid with the fuming acid, so that the strength is brought up to 98 per cent., and then cooling it till some crystals of pure H_2SO_4 are deposited. These crystals can then be used for obtaining a large quantity of the same acid by throwing them into a vessel of concentrated acid cooled to 0° . The mass is stirred and cooled still further until the formation of crystals ceases. After these crystals have been filtered from the mother liquor they melt at the temperature of the room to form the desired hydrate, H_2SO_4 .

Benzidinemonosulphonic acid (Ber. **22**, 2,459), for example, can be obtained by this method only. This substance has acquired great importance from the fact that azo-dyes, which dye unmordanted cotton and resist washing, so-called "substantive" dyes, are derived from it. When fuming sulphuric acid or mixtures which often take its place are used, at least four different benzidinesulphonic acids are formed simultaneously. To prepare the monosulphonic acid, benzidine or, better still, its sulphate (1 part), is mixed with the prepared acid (2 parts) and heated for an hour and a half at 170° . The mass is then poured into water, and the sulphonic acid which separates is filtered off (cf. § 12).

Vignon (Ger. Pat. 32,291) obtained α -naphtholdisulphonic acid by heating α -naphthol with the same acid for eight or ten hours at 100 – 110° .

5. Fuming Sulphuric Acid.—The advantage of using fuming sulphuric acid lies in the fact that all secondary reactions brought about by the presence of water are necessarily excluded. Bender (Ber. **22**, 994) has actually found that some sulphonc acids of α -naphthol even lose sulphonc acid groups, when the temperature rises, under the influence of the excess of sulphuric acid associated with the water originally contained in the acid and that formed by the progress of the action.

Naturally fuming sulphuric acid acts much more vigorously than the ordinary acid, on account of the anhydride which it contains.

For example, Gürke and Rudolph (Ger. Pat. 38,281) find that naphthalenetrisulphonic acid may be obtained by adding naphthalene (1 part) to fuming sulphuric acid containing 24 per cent. of SO_3 (8 parts), and heating the mixture for several hours at 180° . Or the same result is attained by cautiously adding naphthalene (1 part) to fuming sulphuric acid containing 40 per cent. of SO_3 (6 parts), care being taken that the temperature does not exceed 80° , and then heating the mixture on the water bath until all signs of the anhydride disappear.

In order to modify the action of the fuming acid and restrict the number of sulphonc acid groups introduced to the desired number, it may be advisable sometimes to dissolve the substance in pure H_2SO_4 and then add enough fuming sulphuric acid to bring the content of anhydride up to that just necessary to form the product wanted.

Here, as in former cases, it will often be desirable to use the substance in the form of a salt instead of employing the free acid or base, if it belongs to these classes. For example, Witt (Ber. **19**, 578) finds that the action of the acid on free α -naphthylamine is somewhat violent, and the product dark in colour from the presence of black impurities. On the other hand, the interaction progresses very smoothly when the hydrochloride of the base is used. The salt is thoroughly dried and added, in small portions at a time, to the fuming acid, containing 20 to 25 per cent. of anhydride. The vessel is kept in ice or snow during the process. The operation is interrupted before a quantity of the salt sufficient to exhaust the calculated amount of free anhydride has been added, and the resulting mixture is poured into broken ice. The α -naphthyl aminesulphonic acid separates as a slimy clotted mass, and is purified by conversion into the calcium salt.

In case of necessity, heating in a sealed tube may be resorted to.

La Coste and Valeur (Ber. **19**, 996) obtained quinolinedisulphonic acid in this way by heating quinolinesulphonic acid with twice its weight of fuming sulphuric acid at 250° . Lönnies (Ber. **13**, 704) prepared γ -sulphoisophthalic acid [$\text{SO}_3\text{H} : \text{COOH} : \text{COOH} = 1:3:5$] by heating isophthalic acid with strong fuming sulphuric acid at 200° .

Heine (Ber. **13**, 493) obtained the same substance by submitting isophthalic acid, in 10 gram portions, to the action of sulphuric anhydride, heating the mixture gently until it was changed into a dark homogeneous liquid. He attempted to crystallise the substance from water, but obtained nothing but a syrup. Lönnies found that it separated from dilute sulphuric acid in long needles or prisms, a property which belongs to many sulphonic acids.

Barth (Ann. **148**, 33) found that *m*-sulphobenzoic acid could be made by placing dry benzoic acid in a flask and conducting the vapour of pure sulphuric anhydride into it. The vapour was easily obtained by heating the strongest fuming sulphuric acid. During the process the operation was assisted by the large amount of heat developed by the chemical action.

Fischli (Ber. **12**, 616) conducted the vapour of sulphuric anhydride over pulverised toluic acid and found that it was rapidly absorbed, forming a thick paste. By pouring this into water sulpho-*p*-toluic acid $\text{CH}_3 \cdot \text{C}_6\text{H}_3(\text{SO}_3\text{H})\text{COOH}$ was obtained.

Sand seems to be the only substance used for diluting the materials in actions of the present class. Thus Heymann (Ber. **24**, 1,477), in making indigodisulphonic acid, mixed phenylglycocoll (1 part) with ten or twenty times its weight of sand, with the object of preventing local excessive heating of any part of the substance during the addition to the sulphuric acid. The mixture was then thrown into warm (20 – 25°) fuming sulphuric acid containing 80 per cent. of anhydride (20 parts) in such a way that the temperature never rose above 30° . When the interaction was over the product was diluted with sulphuric acid of sp. gr. 1.71, ice was added, and the indigo carmine, the sodium salt of indigodisulphonic acid, thrown down with common salt.

6. Use of Phosphorus Pentoxide or Potassium Sulphate with Sulphuric Acid.—When fuming sulphuric acid was not sufficiently powerful, Barth and Senhofer (Ann. **159**, 217) found that it could be reinforced by the presence of anhydrous phosphoric acid. They prepared disulphobenzoic acid [$\text{COOH} : \text{SO}_3\text{H} : \text{SO}_3\text{H} = 1:3:5$] by warming benzoic acid (10 gr.) with oil of vitriol (20 gr.),

and, when the mixture had cooled, adding glacial phosphoric acid (15 gr.) and very strong fuming sulphuric acid (15 gr.), and heating the mixture in a sealed tube at 250° .

Barth and Herzig (M. f. Ch. **1**, 808) dissolved mesitylene (1 part) in fuming sulphuric acid (10 parts), and heated the solution for from two to three days at $30-40^{\circ}$. At uniform intervals of about ten hours three or four parts of phosphoric anhydride were added. This leisurely procedure was justified by the fact that when the operation was hurried the product was partially or even completely carbonised.

Weidel and Cobenzel (M. f. Ch. **1**, 845) satisfied themselves that, even above 200° , fuming sulphuric acid was without action on cinchoninic acid. But they succeeded in obtaining a yield of 70 per cent. of a monosulphonic acid by heating dry cinchoninic acid (10 gr.) with phosphoric anhydride (20 gr.) and oil of vitriol (20 gr.) at $170-180^{\circ}$ in a sealed tube for six hours.

The use of a sealed tube may often be avoided when pure H_2SO_4 and metaphosphoric acid are used. A mixture of two parts of the former with one of the latter has the same effect as fuming sulphuric acid containing 20 or 25 per cent. of anhydride, yet it emits only traces of the vapour of the anhydride when heated at $280-300^{\circ}$. For example, a rosanilinesulphonic acid is obtained when rosaniline sulphate or chloride (2 parts) is added to a solution of anhydrous metaphosphoric acid (3 parts) in pure H_2SO_4 (7 parts) and the mixture is heated on the water bath, or better at $120-130^{\circ}$, until the product is completely soluble in alkalis.

As has been mentioned already, it is often advisable to use salts instead of free acids. When the potassium or sodium salts are taken, the acid sulphates of the alkali metals, which are formed at once, may be as effective in furthering the action of the sulphuric acid as phosphoric acid has been shown to be.

Benzenetrisulphonic acid (Ann. **174**, 244) was formerly a substance very hard to prepare. It had to be made by heating benzene with fuming sulphuric acid and phosphoric acid in a sealed tube. It may now be obtained by Jackson and Wing's method (Am. Ch. J. **9**, 325) in an open vessel. Benzene-*m*-disulphonate of potassium (15 gr.) is mixed with concentrated sulphuric acid (18 gr.) in a porcelain basin and carefully heated over the naked flame so as not to allow the edges of the liquid to char. After a few minutes the mass becomes pasty and the evolution of vapour becomes less. The yield reaches 44 per cent. of the theoretical

The hydrocarbon itself may also be used as the starting point. In the first place equal volumes of benzene and sulphuric acid are boiled until the former has dissolved. Thereupon an equal volume of concentrated sulphuric acid is added along with an amount of potassium sulphate equal to 70 per cent. of the original benzene used. The mixture is then placed in a retort, without tubulus, and one third of the total sulphuric acid is distilled off and the residue is treated as above.

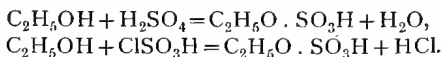
7. Sulphuryl Oxychloride.—One of the difficulties attending the preparation of sulphonic acids is that ordinary sulphuric acid is often too weak, while the fuming acid is, on the one hand, also inadequate, or else, on the other hand, too strong. In such cases sulphuryl oxychloride SO_3HCl is often found to be an efficient substitute. When desirable it can be diluted with chloroform.

Beckurts and Otto (Ber. **11**, 2,058) state that it may be prepared by placing fuming sulphuric acid containing 40 per cent. of anhydride in a retort connected with a well-cooled receiver. The acid is melted, and hydrochloric acid gas is led into it as long as it is absorbed. The product is then distilled off, and, after a second distillation, boils at $149\text{--}151^\circ$. The yield is nearly quantitative. Friedländer (Farbenfabrikation, p. 111) obtains it, diluted of course with concentrated sulphuric acid, by adding common salt to fuming sulphuric acid.

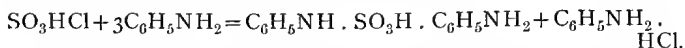
Limpricht (Ber. **18**, 2,172), who made a careful investigation of the matter, found that reactions with sulphuryl chloride went very smoothly with little or no formation of by-products. This reagent, he found, was decidedly to be preferred for making disulphonic acids on account of the time which is lost in their purification when sulphuric acid is used.

The apparatus used by him consisted of a tubulated retort connected by an air-tight joint with a tubulated receiver. The tubulus in the latter was provided with a tube to conduct off the hydrochloric acid gas. That in the retort was either closed with a stopper after the materials had been introduced or with a cork through which a separating funnel passed to serve for the gradual admission of the sulphuryl chloride. The retort was heated to the proper temperature in an oil bath.

As a rule the same products are obtained with sulphuryl chloride as with sulphuric acid. Thus from ordinary alcohol we get, in both cases, ethylsulphuric acid.



From acid amides, however, we get not acids, but acid chlorides, and from amines sulphaminic acids. These exceptions hold both in the fatty and aromatic series. Thus Traube (Ber. **23**, 1,654) prepared salts of phenylsulphaminic acid by dissolving aniline (3 mol.) in several times its volume of chloroform, cooling the solution, and adding gradually sulphuryl oxychloride (1 mol.). A mixture of aniline salts of the sulphaminic acid and hydrochloric acid was at once precipitated.



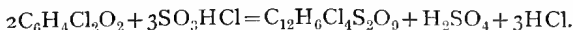
Nitrobenzene (50 gr.) was treated with the calculated amount of the chloride for four hours, the temperature being allowed gradually to rise during this time until it finally reached 150°. Metanitrobenzenesulphonic acid was almost the sole product, just as when sulphuric acid was used.

Toluidinesulphonic acid was prepared in the same way. To avoid charring, the temperature was not permitted to exceed 160°.

Claëssen (Ber. **14**, 307) succeeded in obtaining toluenetrisulphonic acid by mixing toluenedisulphonate of potassium (1 mol.) with sulphuryl oxychloride (3 mol.) and heating them in a flask at 240° until a sample removed from the vessel dissolved completely in water. The mass did not become deeper coloured than pale yellow, and comparative little vapour was given off.

Hodgkinson and Matthews (Ber. **16**, 1,103) state that when dibromofluorene is dissolved in chloroform, and the calculated amount of sulphuryl oxychloride is added, dibromofluorenesulphonic acid is produced.

Reinhard (J. pr. Ch. **125**, 332) mentions a somewhat complicated reaction which took place when finely pulverised dichlororesorcinol (10 gr.) was added to sulphuryl oxychloride (40 gr.), and which was represented by the equation :—



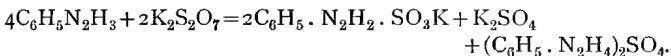
The substance $\text{C}_{12}\text{H}_6\text{Cl}_4\text{S}_2\text{O}_9$ was either the anhydride of a dichlororesorcinolsulphonic acid, or a sulphonic acid containing two dichlororesorcinol molecules. The irregular course of the action was probably due to the presence of the free hydroxyl groups. It would have been advisable to convert the substance into the acetyl derivative before proceeding to make the sulphonic acid.

8. Potassium and Sodium Bisulphates and Pyrosulphates.—Bischoff (Ber. **23**, 1,912) mixed aniline and naphthylamine with potassium bisulphate, and heated the mixtures at 200–240°. The expected sulphonic acids were formed, but the yields were very poor.

Kendall (Am. Pat. 421,049) finds, however, that when rosaniline is mixed with potassium or sodium bisulphate and heated for a sufficient length of time, the desired sulphonic acid can be obtained.

Girard (Bull. Ch. **25**, 333) states that sulphonic acids may be readily prepared by heating the substance with sodium pyrosulphate (free sulphuric acid may be present also) at 200–250°.

No suitable method was known for converting phenylhydrazine into salts of phenylhydrazinesulphonic acid until Fischer (Ann. **190** 97) used potassium pyrosulphate for the purpose. The pyrosulphate is made by heating the bisulphate. When the finely-pulverised pyrosulphate (1 mol.) is mixed with the base (2 mol.) and heated to 80°, the mass completely solidifies in a short time and is then found to contain potassium sulphate, phenylhydrazine sulphate, and potassium phenylhydrazinesulphonate. The latter is secured by dissolving the substances in warm water and removing the greater part of the sulphuric acid with barium carbonate. The greater part of the free base separates as an oil. The warm liquid is filtered and, concentrated caustic potash having been added, the salt of the sulphonic acid crystallises out. It is not yet certain (Ann. **199** 301) whether the action is represented by the following equation or not :—



The yield of ethylhydrazinesulphonate of potassium reached 80 per cent. of that theoretically possible.

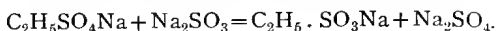
9. Fatty Sulphonic Acids.—All the methods so far described have been applicable to the preparation of aromatic sulphonic acids only. Those of the fatty series are obtained almost exclusively by double decomposition.

As early as 1841 Fehling (Ann. **38**, 286) succeeded in making sulphosuccinic acid by leading sulphuric anhydride over succinic acid at a temperature not exceeding 50°, and allowing the product to remain for twenty-four hours. Hemilian (Ber. **6**, 196) prepared sulphobutyric acid by the action of sulphuryl oxychloride on butyric acid. The oxidation of mercaptans supplies another way of making sulphonic acids. But a method of preparing them easily in large

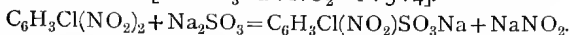
quantities was first found by Strecker (Ann. **148**, 91), and consisted in the action of alkylhalides on sulphites of the alkalis. Mayer (Ber. **23**, 909) has since shown that salts of ethylsulphuric acid can take the place of the former. Hemilian (Ann. **168**, 146) has shown that ammonium sulphite is the most suitable salt, since its use permits of the isolation of the usually very soluble sulphonic acids without much loss. For example, ethyl iodide (20 gr.) is boiled for six hours with crystallised ammonium sulphite (20 gr.) dissolved in water (40 cc.) in a flask attached to a condenser. When the iodide has all gone into solution, the liquid is diluted with water, and is boiled with lead oxide until all the ammonia has been driven off. The lead iodide is removed by filtration, and the lead salt of ethylsulphonic acid contained in the filtrate is decomposed with hydrogen sulphide. The solution is then treated with barium carbonate, and on evaporation gives 22 grams of the barium salt of ethylsulphonic acid (theory = 24 gr.).

10. Use of Alkali Sulphites.—It is an extraordinary fact that ammonium sulphite reacts with nitro-bodies forming sulphonic acids. This was discovered by Piria (Ann. **78**, 31) as early as 1850. Smit (Ber. **8**, 1,443) heated nitrobenzene (60 gr.), ammonium sulphite (170 gr.), and absolute alcohol (1 l.) on the water bath for about thirty hours. To preserve the alkalinity of the mixture he added ammonium carbonate. This was gradually volatilised and collected in the condenser, sometimes stopping it up. When the action was over, he filtered from the ammonium sulphate which had been deposited. When the filtrate cooled, beautiful crystals of the ammonium salt of sulphanilic acid $\text{NH}_2 \cdot \text{C}_6\text{H}_4 \cdot \text{SO}_3\text{NH}_4$ appeared. He prepared the ammonium sulphite in the first place by leading moist sulphur dioxide and excess of ammonia into absolute alcohol (Muspratt).

Mayer placed crystallised sodium sulphite (2 parts) in pressure bottles and dissolved it as far as possible in an equal weight of water. Sodium ethyl sulphate (1 part) was then added. After four hours' heating at $100\text{--}120^\circ$ the contents were emptied into a basin and the sodium sulphate allowed to crystallise. The filtrate was then evaporated to dryness and the residue extracted with 96 per cent. alcohol. This removed the sodium salt of ethylsulphonic acid.

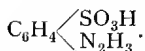


Laubenheimer (Ber. **15**, 597) found that when dinitrochlorobenzene was boiled for several days with excess of sodium sulphite dissolved in water, a nitrochlorobenzenesulphonic acid and sodium nitrite were formed $[\text{Cl} : \text{SO}_3\text{Na} : \text{NO}_2 = 1 : 3 : 4]$.



Erdmann (Ger. Pat. 61,843) states that, in consequence of the fact that a chlorine atom standing in the ortho-position to a nitro-group is easily replaced by other radicals, *m*-nitrobenzaldehyde-*p*-sulphonic acid can be readily prepared on a large scale from *p*-chloro-*m*-nitrobenzaldehyde by boiling it with excess of sodium sulphite in aqueous solution.

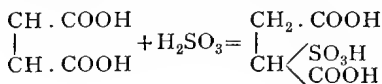
Schmitt and Glutz (Ber. **2**, 51) were the first to prepare sulphonic acids by the action of alkali sulphites on diazo-bodies. Somewhat later Strecker (Ber. **4**, 784) dissolved diazobenzene nitrate in a solution of potassium bisulphite. On evaporating the solution a salt remained, which Fischer's work (Ann. **190**, 73) has since shown to have been the potassium salt of a sulphonic acid derived from phenylhydrazine—



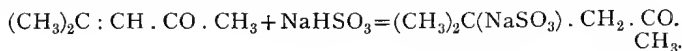
When, however, diazobenzene nitrate is added to a cold neutral or faintly alkaline solution of potassium sulphite, the yellowish-red solution solidifies either spontaneously, or on addition of caustic potash, to a mass of crystals of the potassium salt of diazobenzene-sulphonic acid, $\text{C}_6\text{H}_5 \cdot \text{N}_2 \cdot \text{SO}_3\text{K}$ (Ann. **190**, 73).

The interesting point about the former reaction is that, as Fischer recognised, we have in the product a member of a class of phenylhydrazine derivatives which can be obtained by transformation from diazo-compounds.

Unsaturated bodies have the power of adding themselves to potassium sulphite directly, and so forming saturated sulphonic acids. Thus Messel (Ann. **157**, 15) dissolved potassium carbonate (100 gr.) in water (400 cc.), and treated the solution with sulphur dioxide. He boiled maleic acid (23 gr.) with this solution of neutral potassium sulphite (100 cc.) in a retort attached to a reflux condenser for several hours. When the solution cooled, crystals of sulposuccinate of potassium were deposited—



Pinner states (Ber **16**, 1,727) that when mesityl oxide remains long in contact with a concentrated solution of sodium bisulphite it dissolves, forming the salt of isopropylacetonesulphonic acid—



Similarly phorone forms $\text{C}_9\text{H}_{16}\text{O}(\text{NaHSO}_3)_2 + 2\frac{1}{2}\text{H}_2\text{O}$ under the same circumstances.

Spiegel (Ber. **18**, 1,481) found that many azo-dyes had the power of uniting with bisulphites and forming sulphonic acids. He heated azobenzene with alcohol and a considerable excess of ammonium bisulphite in a pressure bottle in the water bath. At first the whole went into solution, and then turned into a solid mass of crystals consisting of the ammonium salt of a monosulphonic acid of benzidine, $\text{NH}_2 . \text{C}_6\text{H}_4 . \text{C}_6\text{H}_4 . \text{NH} . \text{SO}_3\text{H}$. The action therefore in this case went beyond mere addition, and was accompanied by a molecular change analogous to that characteristic of hydrazobenzene.

Bertagnini (Ann. **85**, 271) was the first to state the now familiar fact that acid sulphites add themselves to aldehydes forming sulphonic acids—



Ludwig (M. f. Ch. **9**, 661) obtained a sulphonic acid of the composition $\text{C}_6\text{H}_{12}\text{O} . \text{SO}_3\text{H}$ by saturating a solution of methyl-ethylacrolein (1 part) in water (3 parts) with sulphur dioxide, and heating the solution in a tube at 80° . He found that sodium bisulphite unites with special ease with unsaturated aldehydes to form sulphonic acids.

11. Use of Carbyl Sulphate.—Both this substance and its chlorhydrin have been suggested for use in preparing sulphonic acids. It seems that sulphonic acids of rosaniline dyes, in particular, may be obtained by heating the materials at 100° until the product is completely soluble in alkalis. The carbyl sulphate, $\text{C}_2\text{H}_4\text{S}_2\text{O}_6$, is made by the union of ethylene with sulphuric anhydride.

The chlorhydrin was prepared by Purgold (Z. Ch. **1868**, 669) by leading ethyl chloride over sulphuric anhydride at 0° . The latter gradually liquefies. The product is heated to 100° , and poured drop by drop into ice-cold water. A heavy oil separates, which is dried

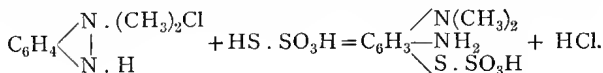
with anhydrous cupric sulphate (Ber. **6**, 502). The yield is 600 grams from 2,000 grams of the anhydride. By fractionation *in vacuo* the pure $\text{C}_2\text{H}_4\begin{smallmatrix} \diagup \text{SO}_2\text{Cl} \\ \diagdown \text{SO}_4\text{H} \end{smallmatrix}$ boiling at $80-82^\circ$ is obtained.

12. Transformation of Acid Sulphates and Alkyl Sulphates of Bases.—The sulphonic acids of many bases may be formed by heating their acid sulphates. Thus Griess and Duisberg (Ber. **22**, 2,458) state that benzinemonosulphonic acid is best prepared by making benzidine sulphate into a thin paste with water, adding sulphuric acid ($1\frac{1}{2}$ mol.) also diluted with water, thoroughly mixing, and then evaporating to dryness. The acid sulphate so obtained is then pulverised and heated for twenty-four hours in an air bath at 170° . The shrunken black mass is again pulverised and extracted with dilute alkali, and the benzinemonosulphonic acid is precipitated from the filtrate with acetic acid.

The acid sulphate of rosaniline is likewise easily converted into the sulphonic acid. Rosaniline (30 parts), sulphuric acid of sp. gr. 1,714 (20 parts), and water (100–200 parts) are thoroughly mixed with sand (400 parts), evaporated to dryness, and heated at $130-140^\circ$. This product, when pulverised and heated at $180-200^\circ$ for five or six hours in a stream of carbon dioxide, and extracted with boiling water, gives the mono- and disulphonic acids.

The sulphonic acids of amides can also be obtained by heating their alkyl sulphuric acid salts at 200° (Ber. **3**, 970). The salt may be prepared by diluting a hot solution of the alcohol in sulphuric acid with water and neutralising with calcium hydroxide, concentrating the filtrate and adding a solution of the oxalate of the base. After filtering again the solution is evaporated to dryness, and the residue heated to the requisite temperature in a small flask. At first some frothing takes place and alcohol is given off. When the mass is cold it is dissolved in hot water, decolourised with animal charcoal, and evaporated until the sulphonic acid begins to crystallise (Ber. **7**, 1,349).

Bernthsen (Ann. **251**, 49) obtained amidodimethylaniline thiosulphonic acid by using aluminium thiosulphate in accordance with equation—



CHAPTER XXIII

REMARKS ON ORGANIC ANALYSIS

1. The Combustion Method.—The general process followed in carrying out a combustion may be assumed to be familiar to the reader and will not therefore be described. Lavoisier was the first (in 1781) to attempt to determine the composition of organic bodies by burning them with oxygen. Whether it is preferable to conduct the operation in a bayonet tube or an open tube, and to use oxygen from the beginning or only towards the end of the combustion are still open questions. It is certain at least that both lead to the same result, though the second may be a little quicker, and in the long run neither seems to have any advantage over the other which gives any prospect that either will be superseded by the other.

In the same way the use of cupric oxide for substances containing no non-metals, and of lead chromate for such as contain them, has not given place to the employment of platinum (Ber. **9**, 1,377), manganese dioxide (Ber. **21**, 3,173), or other compounds which may have been suggested from time to time; nor has the platinum tube displaced the glass tube for ordinary purposes. We owe the employment of cupric oxide to Gay-Lussac, who first used it in 1815. This substance is markedly hygroscopic, so that it should be warm when placed in the tube. Lead chromate possesses the same property (J. pr. Ch. **81**, 184) to about the same extent. According to Ritthausen (J. pr. Ch. **133**, 141) it also retains some carbon when ignited in the air, and this can only be removed by burning in a stream of oxygen. Liebig (Anleitg. z. Anal. org. Körper, 32) recommends the use of a mixture of lead and potassium chromates.

It is a common experience to find that substances containing

much halogen give too high values for carbon (M. f. Ch. **1881**, 111). To secure the more complete removal of the halogens, therefore, a coil of silver is placed in the end of the tube. In the combustion of iodosobenzoic acid (Ber. **25**, 2,632) it was even found necessary to insert several such coils, for, in their absence, some free iodine passed over, even when a very long layer of lead chromate was used. When the coils have become covered with halogen compounds of silver through frequent use, they may be purified by ignition in a stream of hydrogen. Coils of copper are much less effective because, when they become too hot, the halogen compound of copper is volatilised and is carried over into the chloride of calcium tube.

Substances which yield carbon monoxide easily must be burnt with a very long layer of oxide of copper, as otherwise the results may be 3 per cent. too low (Ann. **242**, 27; and Ber. **25**, 408).

Anschütz and Kekulé (Ann. **228**, 303) state that substances intended for combustion should be dried in a Liebig's drying tube. This is placed in an air bath, kept at a suitable temperature, and the drying is carried out either *in vacuo* or in a stream of air or of some indifferent gas. When substances treated in this way give off hydrochloric acid or ammonia, the gases are caught in solutions of known strength and estimated by titration or gravimetrically.

As Liebig himself remarks (Ann. **95**, 259), even substances containing no hydrogen always yield a little water on combustion, and it has not yet been found possible to exclude this source of error. Berzelius was the first (in 1815) to introduce the chloride of calcium tube for weighing the water formed in the analysis.

Lieben has drawn attention to the fact that if long rubber tubes are employed to connect the apparatus for drying the air, and oxygen with the combustion tube, the effect is often almost the same as if the carefully dried gas had been bubbled through water again. He used, therefore, tubes of glass or lead. In this connection the recent work of Berthelot (C. R. **110**, 684) on the removal of traces of moisture from gases may be consulted.

When pulverised compounds have to be mixed with cupric oxide or lead chromate, Thörner recommends that the mixing be effected in a tube made for the purpose. This tube is 12 to 15 cm. long, 10 to 11 mm. in diameter, closed at one end and considerably drawn out at the other, so that it can be conveniently introduced into the combustion tube. The substance is weighed out in a glass tube whose end can be introduced into the mixing tube. The latter

is charged with a layer several centimetres high of cupric oxide or lead chromate, which has been freshly ignited and cooled over sulphuric acid. The substance is thrown in above this, the tube is closed with a cork, and then thoroughly shaken. A little of the oxide or chromate is placed in the combustion tube, the contents of the tube are emptied in above this, and finally all traces of the substance are cleared out of the tube by repeated shaking with small quantities of the oxide or chromate.

The necessity of placing a coil of copper at the end of the combustion tube to decompose any nitric oxide which may be formed has lately been re-examined by Klingemann (Ber. **22**, 3,064). He estimated the amount of nitric oxide formed in the combustion of an azine, $C_{28}H_{16}N_2$, and found that it reached 8.40 per cent. of the quantity of the original substance.

Copper coils are preferable to those of silver for this purpose. In this connection Zincke and Kegel remark (Ber. **23**, 246) that in the combustion of dichloromalonamide the coil of silver did not suffice to decompose all the oxides of nitrogen, and that in consequence the percentage of carbon obtained was too high.

Schulze and Steiger (Z. physiolog. Ch. **11**, 49) found that in analysing arginine nitrate, $C_6H_{14}N_4O_2 \cdot HNO_3 + \frac{1}{2}H_2O$, in spite of the presence of a copper coil, the carbon was always too high and the nitrogen too low. In order to ascertain whether any nitric oxide was escaping from the combustion tube, he replaced the potash bulbs by a similar apparatus filled with ferrous sulphate. No change of colour was observable in the solution, however. On the other hand, the water which condensed in the bulb of the chloride of calcium tube showed a strong acid reaction, which might have been due to the presence of a small amount of nitric acid.

Schwarz (Ber. **13**, 559) states that copper coils which have been reduced in a stream of hydrogen should be gently warmed until a thin outer oxidised layer has been formed. They lose a small amount of hydrogen in the process. It is doubtless better, however, to reduce them in carbon monoxide. The gas can be prepared by the action of sulphuric acid on oxalic acid, and the presence of the carbon dioxide in the gas does not interfere with the reduction.

When salts containing an inorganic base are burned, the latter may retain carbon and carbon dioxide. To avoid this potassium bichromate is placed in the boat. This substance assists in the combustion of the carbon, and drives the carbon dioxide out of its combination with the alkali.

Schwarz and Pastrovich (Ber. **13**, 1,641) mixed an excess of finely divided chromic oxide with the substance. They prepared it by precipitating mercurous nitrate with pure neutral potassium chromate, and, after filtering and washing, ignited the chromate of mercury in a porcelain crucible.

If the substance has a tendency to leave a deposit of carbon which cannot be burned even in a stream of oxygen, the substance, after being placed in the boat, should be covered with three or four times its weight of previously ignited platinum black.

When explosive substances have to be analysed, they must be mixed with sufficient cupric oxide to counteract this tendency.

2. Other Methods for Determination of Carbon and Hydrogen.—No improvement has taken place in the results of the combustion method since 1830, and the enormous amount of time which even experienced workers must devote to such almost mechanical operations is a great disadvantage of the process. It would certainly be a great boon to chemists if some method, like that of Kjeldahl's for nitrogen, could be devised, by which the estimation of carbon and hydrogen could be conducted in the wet way in an apparatus which would not demand constant attention.

It may perhaps be hoped that the investigations of physical chemists may put some weapon in our hands which will be as valuable for the present purpose as the replacement of the complicated methods of determining molecular weights by the freezing- and boiling-point methods has been for another branch of the work of the organic chemist. Possibly in the future some way may be devised—say by the use of compressed oxygen—which will greatly simplify the estimations of carbon and hydrogen, or at least that of the former.

Many years ago Brunner (Pogg. Ann. **95**, 379) described a method of using sulphuric acid and potassium bichromate for determining the carbon as carbon dioxide in the wet way. Messinger (Ber. **21**, 2,910) has recently developed this process more fully, and with further improvement it promises to supply a way of making carbon determinations of every kind. It is given here as an example of wet-way processes.¹

¹ Messinger has more recently (Ber. **23**, 2,756) described an improved form of his apparatus, in which, however, the simplicity which was characteristic of the earlier one has been sacrificed to a certain extent. He

The organic body is placed in an apparatus devised by Classen (Quant. Anal. [3], 239), and heated with sulphuric acid and chromic acid. The carbon dioxide which is formed is swept by a stream of air into a set of potash bulbs. In order that a very small flask may be used, the funnel is fused into the tube which introduces the air.

The evolution of carbon dioxide is often rapid, and it is therefore necessary to connect the potash bulbs with a weighed tube containing soda-lime. Liquids are enclosed in small glass bulbs just as in ordinary combustions.

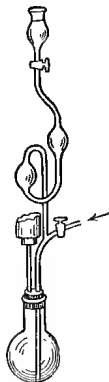


FIG. 41.

To carry out the analysis, chromic acid (5 to 6 gr.) or pulverised potassium bichromate, and a small tube containing the substance (15 to 35 gr.), are placed in the flask. In connecting the flask with the condenser, care must be taken that the substance does not come in contact with the chromic acid. When potassium bichromate is taken, no attention need be paid to this point. A slow stream of air, purified by passing through caustic soda and a tube containing soda-lime is led into the apparatus to expel any carbon dioxide which may be present. While this operation is going on the potash bulbs and soda-lime tube can be weighed. These are then connected with the drying tube filled with glass beads. A chloride of calcium tube must be attached to the soda-lime tube so as to prevent

the entrance of moist air. When everything is in readiness the stream of air is momentarily interrupted, and sulphuric acid (30 cc.) is allowed to enter by the funnel tube. Care must be taken to keep the condenser cool from this stage onwards.

When liquids are analysed, the bulb must be broken with the help of the funnel tube.

The flask is now warmed with a very small flame, which hardly touches the asbestos, placed beneath.

After the lapse of a few minutes a slow evolution of carbon dioxide can be noticed at the surface of the mixture. The flame must be instantly removed, and not replaced until the production of gas has almost ceased. The heating can then be continued to the end of

mentions that when the form described in the text is used, some substances give values for the carbon which are constantly 0.8-1 per cent. too small. It must therefore be noticed particularly that the method is not applicable to all substances,

the operation. The oxidation requires very little attention. The decomposition of the substance occupies two hours. At the end of that time air is driven through the apparatus to remove the oxygen.

If substances which sublime are left out of account, the method will be found frequently to give good results. But care must be taken not to overheat the mixture at first, as otherwise a very violent action takes place, foglike fumes are generated, and the result obtained is too high.

When the substance contains a halogen, a small Drechsel's wash bottle (100 cc.) must be filled with a concentrated solution of potassium iodide, connected with a small U-tube containing glass wool, and inserted behind the condenser. One half of the glass wool must be moistened with a solution of silver nitrate, and the other half, that next to the drying tube, with concentrated sulphuric acid.

Sulphur, phosphorus, and arsenic are oxidised to sulphuric, phosphoric, and arsenic acids respectively. The halogens are given off in the free state.

Cross and Bevan (J. Ch. Soc. **53**, 889) collected the carbon dioxide obtained by this method over mercury, instead of weighing it. Their experience showed that carbon monoxide was always formed to some extent, although the proportion was greater at the beginning of the operation than towards the end. Oxygen is not given off unless the temperature exceeds 100° . The analyses which they publish show that good results may be obtained if a correction is applied for the carbon dioxide absorbed by the sulphuric acid. To do this there must be added to the percentage of carbon a number obtained by multiplying this value by the constant '016. For example¹—

$$C = 43.55 + 43.55 \times .016 = 44.25\%$$

¹ Without paying any attention to the work that has already been done in this field, Okada has recently discovered and made known a method of analysing substances of interest to students of hygiene and physiology such as flesh, milk, uric acid, salicylic acid, &c. He treats them, much as in Kjeldahl's process, with slightly fuming sulphuric acid with addition of substances like mercury. The carbon is converted quantitatively into carbon dioxide (!), and this gas is not weighed in potash bulbs, but caught in baryta water and titrated! The sulphur dioxide, which is formed simultaneously, seems to have the valuable property of being completely removed from the mixture of gases when the latter is passed through a

3. Qualitative Determination of Nitrogen.—The presence of nitrogen can be ascertained by heating the substance with soda-lime in a small tube, and observing whether ammonia is given off or not.

The method employed by Lassaigne (Ann. **48**, 367), however, is much more delicate. The substance is raised to a red heat with potassium or sodium in a small tube. The residue is treated with water, care being taken to avoid harm from flying pieces of the metal, and to the filtrate are added ferrous sulphate, ferric chloride, and, finally, hydrochloric acid. If a blue precipitate is formed, the presence of nitrogen is proved. The cause of the precipitate is, of course, that the nitrogen and sodium in presence of carbon unite to form sodium cyanide. This, with the salts of iron in the alkaline liquid, is converted into sodium ferrocyanide, and the latter gives Berlin blue with the excess of iron when the solution is acidified. Naturally, ammonia and salts of nitric acid must be absent.

Jacobsen (Ber. **12**, 2,317) was the first to call attention to the fact that the method occasionally fails, especially when the organic body contains sulphur along with nitrogen. For example, in the presence of amides of sulphonic acids, thiourea, &c., sodium sulphocyanide is formed. In a few such cases, when the substance is ignited, a carbonised mass remains behind, which contains much of the nitrogen and very little of the sulphur, and the test may succeed with this. But by a slight modification he devised a process, depending on the partial reduction of the sulphocyanide to cyanide, by means of iron, which is in all cases reliable.

A grain of the substance is mixed with four or five times its volume of finely divided iron, and this mixture is fused with potassium or sodium exactly as above. The cold mass is treated with water for a few minutes and filtered. The filtrate is acidified with a few drops of hydrochloric acid, and dilute ferric chloride is added. The iron must be previously tested with sugar, or some other substance which contains no nitrogen, and should give no blue or green coloration.

Gräbe (Ber. **17**, 1,178) states that the ordinary test for nitrogen

layer of saturated permanganate solution several centimetres high. The presence of carbon monoxide and other trifling details were not observed. Finally the author surmises that his method may be used for the determination of the oxygen in organic bodies. Further information will be found in the Archiv. f. Hygiene, **14**, 4, 364-373.

will succeed, even in presence of sulphur, if only a large amount of potassium is used. The excess then exercises the functions of the iron in Jacobsen's method. On the other hand, the presence of nitrogen in diazo-bodies can hardly ever be shown by this method, because the nitrogen escapes before the action of the alkali metal begins.

4. Quantitative Determination of Nitrogen by Combustion.

— Nitrogen is now usually estimated quantitatively by Dumas' or Kjeldahl's methods.

It may be assumed that the reader is acquainted with the general procedure in Dumas' method. The various forms of apparatus suggested for the collection of the nitrogen have been discussed by Ilinski (Ber. **17**, 1,347). The simplest is probably that of a graduated tube provided with a stopcock. It is filled with caustic potash up to the latter by suction. When all the air has been driven out of the apparatus, suction is again applied, and the combustion of the substance is begun. The caustic potash is prepared by dissolving potassium hydroxide (1 part) in water (2 parts). Caustic soda cannot be used. To avoid the passage of any of the liquid into the mouth, a bulb-shaped enlargement should be blown on the tube above the stopcock.

The carbon dioxide can be generated by heating powdered magnesite. Ilinski recommends manganese carbonate, as it is very slightly hygroscopic, gives a uniform stream of the gas, and by turning brown enables one to follow the progress of the decomposition.

Substances which are hard to burn may be mixed with a little mercuric oxide in addition to cupric oxide. Of course, care must be taken to regulate the amount, so that the oxygen will be completely absorbed by the copper coil.

When substances containing nitrogen are decomposed by warm carbon dioxide, or are volatilised by it to any appreciable extent, the gas must not be evolved as described. In this case a Kipp's apparatus is used, and a rather rapid stream is conducted through the tube for a limited time. The rear end of the combustion tube should be drawn out to a capillary.

For example, Fischer (Ann. **190**, 124) mixed phenylhydrazine-carbazolate with pulverised cupric oxide in a small tube, filled the latter up with cupric oxide, and introduced it into the combustion tube. When all the air had been expelled by a rapid stream of cold carbon dioxide, the capillary was sealed off, the tube connected

with the other end of the combustion tube dipping meanwhile under mercury. By cautious tapping, the narrow tube containing the substance was then emptied into the wider combustion tube, and the burning was begun in the ordinary way.

Gehrenbeck (Ber. **22**, 1,694) has recently proposed a way of determining nitrogen and hydrogen simultaneously by a modification of Dumas' method. This process is highly praised by Kehrman and Messinger (Ber. **24**, 2,172).

O'Sullivan states (J. Soc. Chem. Ind. **1892**, 327) that, when Dumas' method is used, from 4 to 11 per cent. of the nitrogen escapes from the tube in the form of nitric oxide.

5. Kjeldahl's Method.—The principle of this method (Z. analyt. Ch. **1883**, 366) consists in heating the substance with a large quantity of concentrated sulphuric acid at a temperature near to the boiling-point of the latter, and finally distilling off the ammonia and estimating its quantity by titration. Various substances are added during the process to assist the oxidation. There is as yet no unanimity on the subject of what compounds are most effective in this respect. Potassium permanganate was first used, and has been succeeded by cupric sulphate and mercury (cf. P. Ar. **46**, 581). More recently Gunning (Z. analyt. Ch. **1889**, 189) has suggested potassium sulphate. This salt and mercuric oxide are both very convenient to use and very effective, so their application is here described.

Gunning uses a mixture made by melting together *potassium sulphate* (1 part) and sulphuric acid (2 parts). The product is semi-solid at ordinary temperatures, but can be easily poured out of warmed vessels. In special cases very large quantities of the substance to be investigated can be analysed. Thus 100 grams of flesh may safely be used if a sufficiently large flask is selected. For ordinary purposes, however, from a half to one gram of the material is placed in a round-bottomed flask with a short wide neck. To this is added 20 to 30 cc. of the mixture described above, and the whole is heated with a Bunsen burner. When the substance is a liquid it is first evaporated nearly to dryness. A little acid can be added to it if necessary during this process.

At first a good deal of frothing is observable, while water with some acid, and later stronger acid, pass off. This loss of acid and concentration of the acid in the flask must not be allowed to go too far. The process is easily regulated, however, for when a funnel,

which fits the mouth of the flask closely, is inserted and is covered with a watch glass, the acid vapours are almost completely condensed and flow back into the vessel.

Arnold and Wedemeyer (P. Ar. 52,590) state that when a mixture of sulphuric acid (3 parts) and potassium sulphate (1 part) is used no considerable frothing occurs.

As soon as the frothing decreases the apparatus can be left to itself. If the flame is so regulated that the evaporated acid condenses and flows down the walls of the flask, carrying carbonised material adhering thereto along with it, the maximum speed attainable by the method will be reached. The product is colourless unless metallic oxides are present which can confer some colour on it. When cold it is dissolved in water.

The time required for the decomposition of the substance is not always the same. Often half an hour suffices, sometimes less; more than one and a half or two hours is never necessary. The analyses published with the description of the method show that excellent results are obtainable.

Mercuric oxide is used by the author (cf. Wilfarth, Centralblatt, 1885, 113) as follows: A flask is selected whose bulb has a capacity of 600 cc. and neck a length of 15 cm. In it is placed a quantity of the substance containing about 0.3 grams of nitrogen. To this is added sulphuric acid containing 15 per cent. of anhydride (7-8 cc.) and some mercuric oxide (.4 gr.). The acid is not drawn up into a pipette but measured in a glass vessel. When first heated on the sand bath the mixture froths considerably, but this ceases entirely after a short time. The heating continues until the liquid becomes colourless. On account of the escape of the sulphur dioxide, formed by the reduction of the sulphuric anhydride, the operation must be conducted under a hood.

The treatment of liquids is precisely similar to that of solids. When urine (10 cc.), for example, is placed in the flask and sulphuric acid and mercuric oxide are added, a considerable rise in temperature takes place. So much dilute acid escapes during the boiling that that which remains is, with the help of the mercuric oxide, fully equal to the task of decomposing the organic matter and converting its nitrogen into ammonia.

The clear liquid which is finally obtained by the treatment with sulphuric acid and mercuric oxide is diluted with water.¹ To the

¹ The liquid obtained in Gunning's process is treated in the same way in every respect, except that relatively more caustic soda is used.

solution 25 per cent. caustic soda (80 cc.) is added. This must be done cautiously so that the very warm liquid remains faintly acid. After the mixture has been cooled in a stream of water the remainder of the alkali is added, as there is then little danger of any of the ammonia escaping. In any case the work must be done rapidly.

The ammonia is then distilled over by boiling vigorously for half an hour. To prevent bumping in the alkaline liquid one or

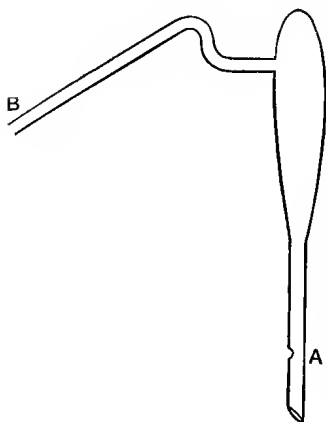


FIG. 42.

two grams of zinc dust are added. The expulsion of the whole of the ammonia can be attained without the residue becoming too concentrated if the apparatus shown in Fig. 42 is used to connect the flask with the condenser. This has also the effect of obviating the possibility of any of the liquid being projected directly into the condenser. The length of this adapter is 25 cm., the diameter at the wider part 3.2 cm. The stem A passes through the stopper of the flask, while B is connected with the condenser.

The opening in the side of the tube near A is a specially valuable feature, as without it the drops of liquid which condense in the apparatus are continually thrown upwards through the whole length of the adapter by the current of vapour. Pieces of granulated zinc cannot here take the place of the zinc dust (P. Ar. 52, 591). They are equally effective in making the ebullition steady, but in this form the zinc does not set ammonia free from a sort of amido-compound which it forms with mercury as the zinc dust does.

When many nitrogen determinations have to be carried out, a flat jacket of sheet tin is used, through which six condensing tubes can pass simultaneously.

Since the reagents which are used, such as sulphuric acid and caustic soda, are never quite free from nitrogen, this correction is determined once for all and is subtracted from the results obtained. With this in view a supply of the reagents sufficient

for a large number of analyses is prepared, and a determination is made with some substance like sugar. This gives the amount of the nitrogen which may be looked for from this source.

The ammonia is collected in a receiver. For this purpose a flask or Peligot's tube is used. This is charged with water to which a slight excess of decinormal sulphuric acid (say 25-50 cc.) has been added. Each centimetre corresponds to '0014 grams of nitrogen. The excess is titrated back with decinormal caustic soda.

As indicator Mays' litmus solution (*Z. analyt. Ch.* **25**, 402) is employed. Ordinary litmus in the granular form (100 gr.) is heated with water (700 cc.) to boiling, and the liquid is decanted. The residue is further boiled with a fresh supply of water (300 cc.). The extracts are united, set aside for one or two days, then acidified with hydrochloric acid, and finally dialysed until the acid cannot be detected in the water any longer. If the water is frequently changed, this may occupy eight days. The solution is preserved in a flask closed with a plug of cotton. As the solution remains at rest for months at a time it continually deposits solid matter, from which it must be freed by filtration; but in spite of this it retains for years the greatest sensitiveness both towards acids and alkalis.

Dafert (*Z. analyt. Ch.* **1888**, 224), who has most thoroughly examined the range of applicability of the Kjeldahl method, has come to the conclusion that substances containing nitrogen may be divided into two classes with respect to it. These are:

(1) Substances which may be submitted to analysis without preparatory treatment, and

(2) Substances which require such preparatory treatment.

To the first group belong amides and ammonium bases, pyridines and quinolines, alkaloids, bitter principles, and albumens and related bodies. Most likely indole derivatives belong to this class.

To the second belong, with isolated exceptions, all nitro-, nitroso-, azo-, diazo-, hydrazo-, and amidoazo-compounds, derivatives of nitric and nitrous acids, hydrazines, and probably also cyanogen compounds.

He gives the following as the most effective treatment which he could devise for nitro-bodies:—If the substance is soluble in alcohol (10 cc.), it is dissolved in this medium (if not, in concentrated sulphuric acid). Zinc dust and sulphuric acid are added, and the mixture is heated until the alcohol has all been expelled.

When this stage is reached ten cubic centimetres of an acid mixture recommended by Kreusler is added and the analysis is carried on as already described. Kreusler's solution is made by mixing rectified concentrated sulphuric acid (1 l.) with phosphoric anhydride (200 gr.) and a little mercury. Dafert found that the nitroso-bodies and an azoxy-compound examined by him, when treated in the same or a similar manner, gave equally satisfactory results.

Chenel (Bull. Ch. [3], 7, 324) states that nitro-derivatives should be reduced with iodine and phosphorus. By reducing nitronaphthalene to naphthylamine, for example, in this way, he found the method gave accurate results.

The description of the application of Kjeldahl's method to the determination of nitric acid (Z. analyt. Ch. 1887, 92) lies beyond the limits of the present work.

Experiments made by L. L'Hôte (C. R. 1889, 817), with a view to comparing the Will-Varrentrapp, Dumas, and Kjeldahl methods as regards their reliability, showed that differences between the results occurred only when the sulphuric acid used for the last failed to become colourless after the heating had continued for a day and a half. The difference was attributed to the volatilisation of a small amount of ammonium sulphate during the prolonged heating.

Nothing on earth is perfect, and even this attractive method seems to share the general fallibility of earthly things. For example, Grünhagen (Ann. 256, 289 and 293) found it unserviceable in the case of methylenedi-*p*-toluidine, $\text{CH}_2 \begin{matrix} \diagup \text{NH} \cdot \text{C}_6\text{H}_4 \cdot \text{CH}_3 \\ \diagdown \text{NH} \cdot \text{C}_6\text{H}_4 \cdot \text{CH}_3 \end{matrix}$, and other bases closely related to it. Yet one might have expected, *a priori*, that the conversion of its nitrogen into ammonia would have been easy. Grünhagen used Dumas' method first, but found the percentage of nitrogen invariably too low. The cause of this might have been found in the retention of some of the nitrogen along with the unburnt carbon. At all events it was found during the combustion of the substance in a stream of oxygen that the last particles of graphite-like carbon were very hard to burn. Yet Kjeldahl's method gave the nitrogen 3 per cent. too low. In the case of this substance the Will-Varrentrapp method (Ann. 39, 257), consisting in the combustion of the substance with soda-lime, was the only one which gave a result in agreement with the calculated figures.

Thiele (Ann. **270**, 56) states that when derivatives of amidoguanidine are analysed by the Kjeldahl method they only give up part of their nitrogen. Amidotetrazotic acid in particular gave only about one fifth of the calculated amount.

6. Determination of Chlorine, Bromine, and Iodine.—The presence of these elements is ascertained by igniting the substance to be tested with quicklime, and examining the solution for calcium chloride, bromide, or iodide in the ordinary way. Substances like chlorobenzene and chlorotoluene, however, are not easily decomposed by lime.

The method devised by Beilstein (Ber. **5**, 620) is more delicate and requires less of the substance. He heats the substance with pure cupric oxide placed in a loop of platinum wire, first in the inner and then in the outer layer of a Bunsen burner flame. The production of a green tinge indicates the presence of halogens, and the persistence of the colour gives some indication of the amount. The test is successful even with very volatile substances like methyl iodide and chloroform.

The *quantitative* estimation of the halogens is attained by igniting the substance in an open tube with quicklime, or by heating it in a sealed tube with nitric acid. Others of the many proposed methods are seldom used.

In using the former process a rather narrow, hard glass tube, 40 centimetres long and closed at one end, is taken. It is charged with first a little quicklime, then a mixture of this with the substance, and finally more lime. The lime must be free from chlorine. When the ignition, which must begin at the open end, is completed, and the tube has cooled, the contents are dissolved in dilute nitric acid and the halogen estimated in the usual manner.

As substances containing iodine may give rise to iodic acid or free iodine, some sulphur dioxide is added before the silver nitrate in such cases.

The use of nitric acid in a sealed tube was introduced by Carius (Ann. **136**, 129). The tube, which should be of potash glass, may be half a metre long, and will then serve for from four to six determinations. It should possess an internal diameter of 13 mm., and the walls should be 1.5–2 mm. thick. The nitric acid must have a sp. gr. as near to 1.5 as possible, corresponding to about 90 per cent. of HNO_3 . When a liquid or other substance on which nitric acid acts violently is being analysed, it should be

weighed out in a small tube about 10 cm. long, and introduced into the large tube enclosed in this manner. From '2 to '3 grams of the substance and 3-4 grams of nitric acid are taken. For fatty bodies a temperature of 150-200° suffices; for those of the aromatic series a temperature of 250-260° must be maintained for an hour and a half. A slight excess of solid silver nitrate is added so that it may unite at once with the halogen.

If the substance is a liquid and has, for any reason whatever, to be weighed in a small glass bulb, this must finally be weighed along with the silver salt. The bulb should in this case be made of hard glass, as if it is made of soda glass (Tollens, *Ann.* **159**, 95) it will lose so much alkali during the heating with nitric acid that a considerable error will be introduced into the result.

Silver iodide retains silver nitrate with great persistency, and must therefore be boiled repeatedly with water before being placed on the filter.

If the organic body contains more than one of the halogens, their separation must be effected by the usual methods of inorganic analysis.

Recently a modification by Schiff (*Ann.* **195**, 293) of Piria's method, in which an open vessel is employed, has come into use.

The substance containing chlorine or bromine, which should not be very volatile, is weighed into a platinum crucible as large as a thimble, and the rest of the vessel is filled up with a mixture of dry sodium carbonate (1 part) and quicklime (4-5 parts). This small vessel is then placed in an inverted position at the bottom of a larger crucible. The annular space between them is then filled with the same mixture. By heating the arrangement with a pointed blowpipe flame it is rendered certain that a part of the mass will become red-hot before decomposition begins to take place. The total quantity of material used in one analysis amounts to about 14 grams. The mass is easily dissolved out of the large crucible.

When the substance contains iodine, sodium carbonate must be used alone, because, in the presence of lime, calcium iodate would be formed. The production of this salt would add greatly to the difficulty of carrying out the analysis.

7. Estimation of Sulphur.—The best quantitative tests for sulphur are probably those of Vohl (*Z. analyt. Ch.* **1863**, 442) and

Horbaczewski (Z. physiolog. Ch. **6**, 331). The former heats the substance with sodium, dissolves the product in water, and tests for the presence of sulphide in the filtrate with sodium nitroprusside. When sulphur is present a bluish-violet coloration is observed. The latter proved the absence of sulphur in elastin by dissolving two grams of that substance in boiling concentrated caustic potash, and saturating the cold solution with chlorine. The product is then acidified with hydrochloric acid, and boiled until chlorine is no longer evolved. If after barium chloride has been added and the solution has remained for two days no trace of a precipitate is visible, the absence of sulphur is demonstrated.

Neither of these methods gives any information as to the state of combination of the sulphur. To test this Vohl (Ber. **9**, 876) uses a special solution. He heats water with twice its volume of pure glycerol to the boiling-point, and adds freshly prepared calcium hydroxide in small quantities till the liquid is saturated with it. He then adds excess of fresh lead hydroxide or of litharge and boils gently for a few minutes. The solution when cold is decanted from undissolved substance, and kept in a bottle so that access of carbon dioxide is avoided.

When substances containing sulphur, such as hair, taurine, etc., are warmed with this liquid, lead sulphide is formed, and the mixture darkens. But no interaction takes place with bodies which contain sulphur united to oxygen.

The *quantitative* determination of sulphur is carried out by Carius' method (Ann. **116**, 1) with nitric acid exactly as described for halogens. With aromatic sulphonic acids however the heating must be carried to 300°. In cases like this, the danger that the tube will burst is avoided by first heating to 200° only, allowing the tube to cool, and letting the accumulated gas escape. After re-sealing, the heating can be continued up to the higher temperature. The sulphuric acid formed is weighed as barium sulphate.

Höland (Ch. Z. **1893**, 991) has made a comparison of all the methods which have been suggested. He recommends the use of moderately concentrated nitric acid, and states that with substances which are easily oxidisable and do not contain too much carbon, this method gives by far the most reliable results. It fails however when the substance contains much carbon or is hard to oxidise. No matter how gradually and regularly the temperature is raised, it seems to be impossible to make it high enough for the purpose

without explosion. Raising it degree by degree, does not seem to do away with this evil, nor does frequent opening to relieve the pressure seem to make any difference. It is evident that a rapid decomposition, accompanied by generation of carbon dioxide, occurs at some stage in the process and bursts the tube.

Gabriel (Ber. **22**, 1,154) had to modify this method in the analysis

of μ -methylmercapto- ϵ -thiazoline, $\begin{array}{c} \text{CH}_2 - \text{S} \\ | \qquad \diagup \\ \text{CH}_2 - \text{N} \qquad \text{C} \cdot \text{S} \cdot \text{CH}_3 \end{array}$, which con-

tained 48.12 per cent. of sulphur. It was first heated for three hours at 200° with fuming nitric acid. The liquid was then concentrated, neutralised with potassium carbonate, evaporated to dryness, and finally fused with soda and potassium chlorate. When the fusion was omitted, only half of the sulphur was converted into sulphuric acid, and the remainder formed methanesulphonic acid, a very stable substance. A process of the same nature had already been described by Arendt,¹ and recommended for use in the estimation of sulphur in plant ashes.

When the substance under examination is not volatile, it can be fused with potassium chlorate, or potassium nitrate and carbonate directly. The sulphur is converted into sulphate, which can then be precipitated in the usual way.

Messinger (Ber. **21**, 2,914) describes another method which gives good results with most, though not with all, comparatively involatile compounds. A weighed quantity of the substance is placed with potassium permanganate (1½–2 gr.) and pure potassium hydroxide (½ gr.) in a flask of 500 cc. capacity connected with a reflux condenser. Some water (25–30 cc.) is then poured in through the condenser tube, and the mixture is heated for two or three hours. The liquid when cold should have a faint red tint. Hydrochloric acid is then added in small portions, and the liquid warmed when the first evolution of gas has ceased after each addition. This treatment is continued until the liquid becomes clear. The contents of the flask are finally washed out into a beaker, and the sulphuric acid precipitated with barium chloride. In order that the barium sulphate may be easily collected on a filter, both the chloride and the liquid must be boiling when mixed.²

¹ "Wachstum der Haferpflanze." Leipzig, 1857, p. 28.

² Cf. Lunge, "Sodaindustrie," Braunschweig, 1879, I. 93.

The combined sulphur can be oxidised in many cases by dissolving the substance in glacial acetic acid, and adding potassium permanganate in small quantities until the operation is complete.

A detailed comparison of many methods of estimating sulphur has been published by Hammarsten (*Z. physiolog. Ch.* **9**, 273), and his paper should be consulted in the original.

DATES OF REFERENCES

To find the year in which any volume of the chief journals mentioned in the text appeared—

Am. Ch. J.—Add the number of the volume to 1878.

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185-190 .	. . 1877	243-248	1888
191-194 .	. . 1878	249-255	1889
195-199 1879	256-260 .	1890
200-205 .	. . 1880	261-266	1891
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211-215	1882	272-277	1893
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- Z. physik. Ch.—Vol. 1 (1887). Vol. 2 (1888). For vols. 3-12 divide by 2 and add to 1887. Vols. 13-15 (1894).
- Z. physiolog. Ch.—Vol. 1 (1878). Vols. 2, 3 (1879). For vols. 4-18, add the number of the volume to 1876.

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